Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Regulatory Decision Document PRDD2004-01

Tepraloxydim
Equinox EC
Dash HC

The active ingredient tepraloxydim, the associated end-use product Equinox EC and the adjuvant Dash HC for the control of annual and perennial grasses in flax, dry peas and lentils in the Prairie Provinces and the Peace River District of British Columbia are proposed for registration under Section 13 of the Pest Control Products (PCP) Regulations.

This Proposed Regulatory Decision Document (PRDD) provides a summary of data reviewed and the rationale for the proposed full registration of these products. The Pest Management Regulatory Agency (PMRA) will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to the Publications Coordinator at the address below.

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Foreword

The submission for the full registration of the active ingredient (a.i.) tepraloxydim, the end-use product Equinox EC and the adjuvant Dash HC, a herbicide developed by BASF Canada for use on lentils, dry peas and flax against annual and perennial grasses has been reviewed by the Pest Management Regulatory Agency (PMRA).

The PMRA has carried out an assessment of available information in accordance with Section 9 of the Pest Control Products (PCP) Regulations and has found it sufficient pursuant to Section 18(*b*) to allow a determination of the safety, merit and value of the active ingredient tepraloxydim, the end-use product Equinox EC and the adjuvant Dash HC. The Agency has concluded that the use of the active ingredient tepraloxydim, the end-use product Equinox EC and the adjuvant Dash HC in accordance with the label has merit and value consistent with section 18(*c*) of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18(*d*). Therefore, based on the considerations outlined above, the use of the active ingredient tepraloxydim, the end-use product Equinox EC and the adjuvant Dash HC are proposed for full registration, pursuant to Section 13 of the PCP Regulations.

Methods of analysis of tepraloxydim residues in various environmental media can be provided to monitoring agencies and research institutions upon request to the PMRA.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

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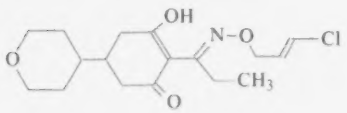
1.0 The active substance, its properties and uses

1.1 Identity of the active substance and impurities

Active substance		Tepraloxydim
Function		Herbicide
Chemical name		
1.	International Union of Pure and Applied Chemistry (IUPAC)	(EZ)-(RS)-2-{1-[(2E)-3-chloroallyloxyimino]propyl}-3-hydroxy-5-perhydropyran-4-ylcyclohex-2-en-1-one
2.	Chemical Abstracts Service (CAS)	(E)-2-[1-[[(3-chloro-2-propenyl)oxy]imino]propyl]-3-hydroxy-5-(tetrahydro-2H-pyran-4-yl)-2-cyclohexen-1-one
CAS number		149979-41-9
Molecular formula		$C_{17}H_{24}ClNO_4$
Molecular weight		341.8
Structural formula		
Nominal purity of active		98% (limits: 95.1–100%)
Identity of relevant impurities of toxicological, environmental or other significance		The technical grade tepraloxydim does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances.

1.2 Physical and chemical properties of active substances and end-use product(s)

Technical product: Tepraloxydim Technical

Property	Result	Comment
Colour and physical state	White crystalline powder	NA
Odour	Odourless	NA
Melting point or range	72.5–74.4°C	NA

Property	Result	Comment
Boiling point or range	NA	NA
Density	1.284 g/cm^3	
Vapour pressure	2.7×10^{-7} hPa at 25°C	Tepraloxydim is non-volatile under field conditions
Henry's Law constant	8.744×10^{-9} kPa·m^3/mol	
Ultraviolet (UV)–visible spectrum	λ (nm) / ε (l×mol^{-1}×cm^{-1}) 204 — 9.5×10^3 225 — 4.6×10^3 258 — 1.1×10^4 290 — 6.8×10^3 300 — 3.1×10^3 Not expected to absorb UV at λ >350 nm.	Teparloxydim has a potential for phototransformation in the environment
Solubility in water at 20°C	pH / Solubility (g/L) 6.5 (water) — 0.43 9.0 — 7.25	Tepraloxydim is very soluble in water under environmentally relevant pH conditions
Solubility in organic solvents	Solvent / Solubility (g/100 mL) acetone — 70.0 methanol — 33.0 2-propanol — 16.0 ethyl acetate — 69.0 acetonitrile — 77.0 dichloromethane — 119.0 toluene — 82.0 n-heptane — 1.0 1-octanol — 15.0 olive oil — 8.0	NA

Property	Result		Comment
Octanol–water partition coefficient (K_{ow}) at 25°C	pH pure water 4 7 9	Log K_{ow} 1.5 2.44 0.20 -1.15	Tepraloxydim has a low potential for bioconcentration/ bioaccumulation in organisms
Dissociation constant (pK_a) at 25°C	pK_a = 4.58		
Stability (temperature, metal)	Stable at 54°C for 14 days Reacted with iron acetate to form black liquid		

End-use product: Equinox EC herbicide

Property	Result
Colour	Dark yellow
Odour	Moderately aromatic
Physical state	Liquid
Formulation type	Emulsifiable concentrate
Guarantee	200 g/L (limits 189.9–210.5 g/L)
Formulants	The product contains a USEPA List 2 formulant at 69.8%.
Container material and description	High-density polyethylene (HDPE) containers with inner barrier (e.g., polyamide) and with foil seal, 2.67 L
Specific gravity	1.032 at 20°C
pH	3.9 (1.0% in pure water)
Oxidizing or reducing action	The end-use product (EP) is a very mild reducing agent and should not be mixed with or stored in close proximity to strong oxidizing agents such as $KMnO_4$. The EP does not react significantly with water or CO_2 and will not increase the hazardous potential for use to extinguish fire. EP does not react with zinc or iron. Special precautions against reducing agents are not necessary.

Property	Result
Storage stability	The product is stable for 12 months at 20°C, 50% RH in polyamide-lined HDPE bottle.
Explodability	Not explosive

1.3 Details of uses and further information

Tepraloxydim belongs to the general class of herbicides termed cyclohexanediones. The primary mode of action is through inhibition of acetyl CoA carboxylase (ACCase), which impacts fatty acid biosynthesis and lipid metabolism. In addition, the cell membrane functions are blocked and cell division is affected. Sensitive grass species exhibit symptoms within a few days in the form of cessation of growth and development. The young leaves turn yellow within 7–21 days and some grass species develop a reddish colouration. Necrotic spots then form on the leaves, leading to subsequent death.

Tepraloxydim is formulated in one end-use product. Equinox EC herbicide is an emulsifiable concentrate formulation with a guarantee of 200 g/L of tepraloxydim that must be applied with the adjuvant Dash HC.

Equinox EC is a selective herbicide for use as a postemergence application to flax (including low linolenic acid and sulfonyl urea tolerant varieties), lentils and dry peas grown in the Prairie Provinces and the Peace River region of British Columbia for the control of specific grass weeds. Equinox EC must be applied with Dash HC adjuvant at 0.41–0.62% volume/volume (v/v [i.e., 0.41 L Dash HC/100 L spray solution]) in a spray volume of 100 L/ha with a maximum of one application per year using ground equipment only.

There are two rates of application for Equinox EC. Equinox EC applied at a rate of 0.165 L/ha (33 g a.i./ha) plus Dash HC adjuvant at 0.41% v/v is effective for the control of wild oats (*Avena fatua*), green foxtail (*Setaria viridis*), volunteer barley (*Hordeum vulgare*) and volunteer wheat (*Triticum aestivum*) at the 1–6 leaf stage up to 2 tillers. Equinox EC applied at a rate of 0.250 L/ha (50 g a.i./ha) plus Dash HC adjuvant at 0.62% v/v is effective for the control of quackgrass (*Agropyron repens*) at the 3–6 leaf stage as well as the above listed annual grass weeds when weed densities are high and overlapping, when staging is late or when weeds are under stress and not growing as actively due to moisture or temperature stress.

Based on the limited data provided, the rate of 0.125 L/ha (25 g a.i./ha) + Dash HC adjuvant at 0.41% v/v may be sufficient to provide acceptable control of the annual grass weeds listed on the Equinox EC label. Prior to an expansion of the use pattern beyond that accepted under this evaluation, efficacy data must be submitted in order to establish the lowest effective rate (LER) for the control of the annual grass weeds listed on the Equinox EC label. Treatments should include the currently accepted application rate of 33 g a.i./ha (1× rate) and lower rates such as 25 and 30 g a.i./ha.

There are no rotational cropping restrictions necessary for Equinox EC.

Equinox EC plus Dash HC adjuvant may be tank mixed with Buctril M (MCPA + bromoxynil) at 1.0 L/ha or Flaxmax (MCPA + clopyralid) at 2.0 L/ha when applied to flax.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

A reversed phase high-performance liquid chromatography/ultraviolet (HPLC/UV) method was provided for the determination of the active ingredient, tepraloxydim, in the technical product. Based on the validation data and the chromatograms provided, the method was assessed to be sufficiently specific, precise and accurate.

2.2 Method for formulation analysis

A reversed phase HPLC/UV method was provided for the determination of tepraloxydim present in Equinox EC herbicide. Based on the validation data and the nature of formulants present, the method was assessed to be specific, precise and accurate for use as an enforcement analytical method.

2.3 Methods for residue analysis

The methods developed by the petitioner for plants (Figure 2.3.3.1) and animals (Figure 2.3.4.1) are common moiety methods designed to determine the total residues of tepraloxydim and its metabolites.

2.3.1 Methods for environmental residue analysis

2.3.1.1 Analytical methodology (parent compound and transformation products)—soil

Three chromatographic methods were submitted for the determination of residues of the parent compound, tepraloxydim (BAS 620 H), and its major transformation products, DP-6, GP, BH620-FP, DP-1 and DP-2, in soil. Based on the validation data and the chromatograms provided, the methods were assessed to be sufficiently sensitive, precise, accurate and specific for the determination.

2.3.1.2 Analytical methodology (parent compound and transformation products)—sediment

Two chromatographic methods were provided for the determination of residues of the parent compound, tepraloxydim (BAS 620 H), and its major transformation products, DP-6, GP, CP-1 and DP-2, in sediment. Based on the validation data and the chromatograms provided, the methods were assessed to be sufficiently sensitive, precise, accurate and specific for the determination.

2.3.1.3 Analytical methodology (parent compound and transformation products)—water

Two chromatographic methods were provided for the determination of the parent compound (BAS 620 H) and its major hydrolysis products, DP-6, GP, DP-1 and DP-2, in pond water. Based on the validation data and chromatograms provided, the methods were assessed to be sufficiently sensitive, precises, accurate and specific for the determination.

2.3.1.4 Analytical methodology (parent compound and transformation products)—biota

In lieu of specific analytical methods for plant and animal matrices, the applicant provided a method for the determination of the residues of the parent compound and its metabolites, 5-OH-DP in soybean seed, forage and hay, as well as a method for the determination of the residues of the parent compound and its metabolites, 5-OH-DP and DL, in hen muscle, liver and fat. Based on the validation data provided, the methods were acceptable and they were extended to the residue methods for plant and animal matrices.

2.3.2 Multiresidue methods for residue analysis

United States Food and Drug Administration (USFDA) Multiresidue Methods (MRMs) published in the *Pesticide Analytical Manual* (PAM, Vol. 1, 3rd edition, 1/94) were used to test tepraloxydim, 5-OH-DP, DL and GP. Based on the chemical structures of the test compounds, Protocols designated as A, B, C, D, E and F from PAM (Vol. 1) were followed. As described below, none of the analytes were recovered efficiently in the protocols in the PAM (Vol. 1) Multiresidue Methods.

Protocol A: Tepraloxydim and its metabolites were not tested through Protocol A as these compounds do not possess an N-methylcarbamate structure.

Protocol B: This protocol contains procedures applicable to pesticides that contain a carboxylic acid or a phenolic moiety. As the metabolite GP possesses a carboxylic acid moiety, it was evaluated through Protocol B. However, the methylated product of GP (GP methyl ester) did not produce a sufficient response on any of the appropriate DG modules tested under Protocol C; therefore, no additional work was performed on this compound under Section 402.

Protocol C: This Protocol contains procedures for developing gas chromatography (GC) data to be added to the tables in PAM Vol. 1, Appendix 1, PEST DATA. Tepraloxydim and its metabolites were dissolved in acetone and tested using various GC columns (DB-1, DB-17 and DB-225) with electron capture detection (ECD), nitrogen-phosphorus detection (NPD), or electrolytic conductivity detection in nitrogen (ELCD-N) or halogen (ELCD-X) modes.

Tepraloxydim and the metabolites 5-OH-DP and DL eluted from each of the GC columns tested and gave a fair to good response with ECD, a fair response with ELCD-N, a weak or poor response with NPD and no response with ELCD-X. Based upon these responses, tepraloxydim, 5-OH-DP and DL were evaluated for recovery through Florisil clean-up (Protocol E) using either a DB-17 or DB-225 column with ECD.

GP and its methyl ester exhibited only a poor response to ECD; therefore, no additional testing was conducted on these compounds.

Protocol D: Evaluation of tepraloxydim and the metabolites 5-OH-DP and DL through Protocol D was not attempted because (i) response of these compounds using an element-selective detector was insufficient to allow for quantitation at the required spiking levels (0.05 and 0.25 ppm) and (ii) although the response of these compounds to ECD would normally allow for detection at the required spiking levels, none of these compounds are recovered from the Florisil clean-up step that is required prior to ECD analysis.

Protocol E: Analysis of tepraloxydim and its metabolites 5-OH-DP and DL using GC (DB-17)/ECD indicated that recovery of these compounds was <30% from Florisil columns using either the mixed ether or methylene chloride elution system. As recoveries from Florisil were <30%, no additional work was performed on these compounds under Protocol E.

Protocol F: As tepraloxydim and its metabolites were not recoverable from Florisil at a level ≥30% using either the mixed ether or methylene chloride elution system in Protocol E, no additional work was performed on these compounds under Protocol F.

2.3.3 Methods for residue analysis of plants and plant products

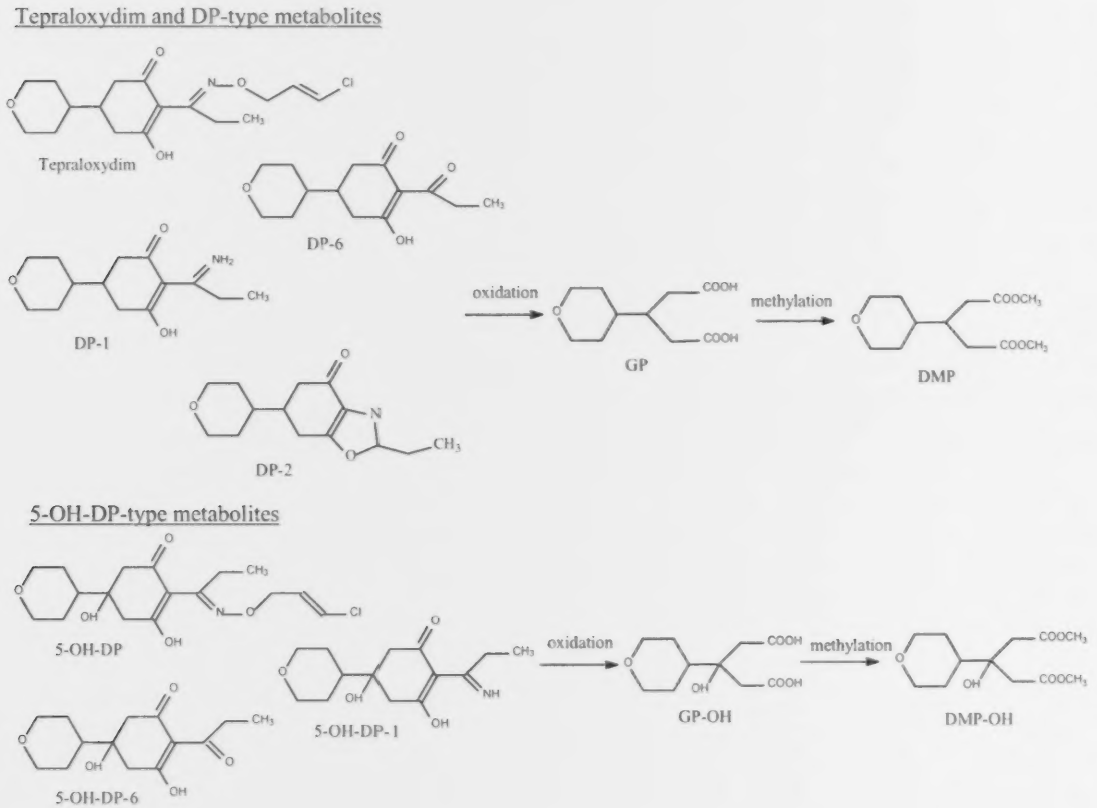
The residue of concern (ROC) for enforcement and risk assessment purposes was defined as parent and metabolites containing the 3-tetrahydropyranylpentane-1,5-dione moiety that are oxidized to GP (or DMP following methylation of GP) plus 5-OH-DP and related 5-hydroxy-metabolites containing the 3-hydroxy-3-tetrahydropyranylpentane-1,5-dione moiety that are oxidized to OH-GP (or OH-DMP following methylation of OH-GP). The petitioner submitted three analytical methods for the analysis of the ROC, as defined above, for plants. In one method (D9704/1), the common moieties GP and OH-GP are anayzed by LC/MS/MS following oxidation; in the other two methods (Method 587 and D9701/1), the common moieties DMP and OH-DMP are analyzed by GC/MS following oxidation and methylation. The reaction schemes for the common moiety methods for plants are shown in Figure 2.3.3.1.

On the basis of the metabolism study for tepraloxydim in/on soybeans, the petitioner submitted a fourth analytical method (Method No. 620-DD-F) for the analysis of the DD metabolite in soybean seed. However, DD was not included in the ROC. The rationale for this decision is discussed subsequently in the residue summary (Section 4.1).

Method 587, a data gathering method, is a common moiety method for the analysis of the combined residues of tepraloxydim (and related DP-type metabolites) plus 5-OH-DP (and related hydroxy metabolites). Briefly, residues are extracted with MeOH and distilled water from soybean (seed, forage, hay, meal and hulls). The extracts are then concentrated to remove the MeOH, and isopropanol and water are added to the concentrate. Calcium hydroxide is added to precipitate plant co-extracts prior to oxidation using hydrogen peroxide. After phase separation by salting out, two kinds of glutaric acids, GP and OH-GP, are isolated from the aqueous layer by charcoal adsorption. The isolates are subsequently converted to their dimethyl ethers, DMP and OH-DMP, by refluxing in sulfuric acid and MeOH. The formed esters are partitioned into DCM and purified by Florisil and C_{18} column chromatography. For soybean crude and refined oil, residues are diluted in hexane, partitioned into ACN, concentrated to dryness and redissolved in isoproponal:water (1:1, v/v). Following precipitation and oxidation, the extracts containing GP and OH-GP are cooled and concentrated. The pH is increased to ~8. The residues are then partitioned with DCM and purified on an NH_2 Sep-Pak and a C_{18} Sep Pak column. In all fractions, the derivatized residues of tepraloxydim and its metabolites are analyzed using GC/MS with select ion monitoring (m/z 182 for DMP and 175 for OH-DMP). The validated limit of quantitation (LOQ) for the combined residues of tepraloxydim is 0.10 ppm for soybean commodities (0.05 ppm for DMP and 0.05 ppm for OH-DMP).

For method validation, samples of soybean matrices were spiked with tepraloxydim or 5-OH-DP at levels that ranged from 0.05 to 25.0 ppm. Overall method recoveries for soybean matrices were 60–116% for tepraloxydim and 60–120% for 5-OH-DP. Although there were some samples with recoveries that were <70%, this occurred in 2 out of 18 samples. Samples of soybean seed were also spiked separately with DP-1, DP-2 and GP at levels that ranged from 0.05 to 2.0 ppm. Overall recoveries for DP-1, DP-2 and GP ranged from 72 to 112% (n=6). Apparent residues were <0.05 ppm (LOQ) in/on all soybean control samples.

Figure 2.3.3.1 Reaction schemes for common moiety analytical methods for plants



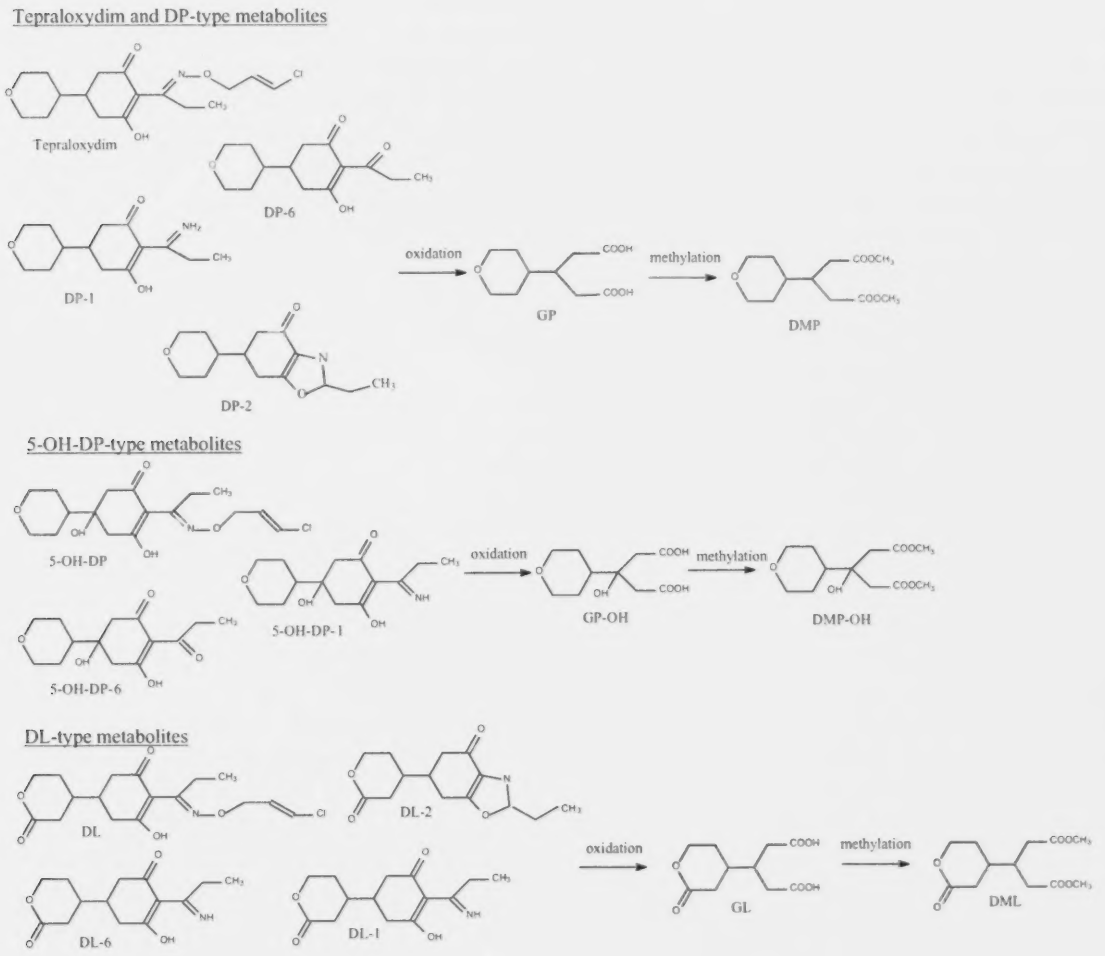
Method D9701/1 is a common moiety method that is similar to Method 587, except that silica gel chromatography replaces Florisil column clean-up. The derivatized residues of tepraloxydim and its metabolites are analyzed using GC/MS with select ion monitoring (m/z 168, 182, 213.1 for DMP and 143, 175 for OH-DMP). The validated LOQ for the combined residues of tepraloxydim is 0.4 ppm for soybean seed and hulls (0.2 ppm for DMP and 0.2 ppm for OH-DMP). The validated LOQ for the combined residues of tepraloxydim is 0.10 ppm for cotton and soybean (other than seeds and hulls) commodities (0.05 ppm for DMP and 0.05 ppm for OH-DMP). Samples of soybean seed that were spiked at 0.2 and 2.0 ppm concurrently with tepraloxydim and 5-OH-DP showed recoveries that generally ranged from 70 to 120%. The exceptions were 4 out of 26 samples spiked with tepraloxydim and 5 out of 26 samples spiked with 5-OH-DP that were outside of the 70–120% acceptable range. Samples of cotton raw agricultural commodity (RAC) were spiked concurrently with 0.05–0.5 ppm (cotton seed) and 0.05–2.0 ppm (gin trash) of tepraloxydim and 5-OH-DP. Recoveries ranged from 65 to 115% for cotton seed and gin trash samples that were spiked with tepraloxydim (7 out of 35 samples tested were outside of the 70–120% acceptable range). Recoveries ranged from 61 to 106% for cotton seed and gin trash samples that were spiked with 5-OH-DP (6 out of 34 samples were outside of the 70–120% acceptable range).

Method D9704/1 is the data gathering method that was proposed as the enforcement method. It is similar to Method Nos. 587 and D9701/1, except that the two common moiety acids, GP and OH-GP, are analyzed by LC/MS/MS. The LOQ is 0.10 ppm (0.05 ppm for GP and 0.05 ppm for OH-GP). For validation, samples of canola seed, soybean seed, dry pea seed and dry pea forage were spiked with tepraloxydim and 5-OH-DP at 0.05–2.0 ppm. Individual recoveries were 69–124% for canola seed (3 out of 28 samples were outside of the 70–120% range), 57–105% for soybean seed (4 out of 24 samples were outside of the 70–120% range), 72–103% for 22 samples of dry pea seed and 61–102% for dry pea forage (2 out of 23 samples were outside of the 70–120% range). An interlaboratory validation study was conducted to determine the reproducibility of the enforcement method. In the interlaboratory validation study, samples of canola seed were spiked with tepraloxydim and 5-OH-DP at 0.05 to 0.20 ppm, and acceptable recoveries (70–120%) were obtained.

2.3.4 Methods for residue analysis of food of animal origin

For animal matrices, the ROC for enforcement and risk assessment purposes was defined as the parent and metabolites containing the 3-tetrahydropyranylpentane-1,5-dione moiety that are oxidized to GP (or DMP following methylation of GP), 5-OH-DP and related 5-hydroxy-metabolites containing the 3-hydroxy-3-tetrahydropyranylpentane-1,5-dione moiety that are oxidized to OH-GP (or OH-DMP following methylation of OH-GP), and DL-type metabolites that are oxidized to GL (or DML following methylation of GL). The petitioner submitted three analytical methods (Method Nos. 389/0, 780 and 975/1) for the analysis of the ROC, as defined above, for animals. In all three methods, the common moieties DMP, OH-DMP and DML are analyzed by GC/MS. The reaction schemes for the common moiety methods for animals are shown in Figure 2.3.4.1.

Figure 2.3.4.1 Reactions schemes for common moiety analytical methods for animals



Method 389/0 is a common moiety method that was developed for milk, cream and liver. For milk and cream, residues of tepraloxydim and its metabolites are extracted with ACN:hexane (3:1, v/v), filtered and allowed to separate into the ACN phase. The hexane is discarded, the remaining residues are partitioned with hexane and the remaining ACN is removed by rotary evaporation. Residues in liver are extracted with MeOH and MeOH:water (1:1, v/v), filtered and concentrated to remove the MeOH. The residues are diluted with isopropanol:water. For all three matrices, impurities are removed by $Ca(OH)_2$ precipitation. The residues are oxidized to yield the GP, OH-GP and GL acids. Following removal of the isopropanol and clean-up on a Mega Bond C_{18} column and an ion exchange (NH_2) column, residues are derivatized in an acidified MeOH solution. Following purification on a silica gel column and an SPE phenyl column, the residues are partitioned with DCM, filtered, concentrated to dryness and brought to volume in acetone. Residues are then analyzed using GC/MS with select ion monitoring (DMP: 182, 162 m/z; OH-DMP: 175, 143 m/z; and DML: 160, 99 m/z) and expressed as parent using molecular weight conversion factors. The reported LOQ for tepraloxydim, 5-OH-DP and DL is 0.01 ppm each in milk, and 0.05 ppm each in liver. For method validation, control samples of liver were spiked with tepraloxydim, 5-OH-DP and DL, each at 0.05 or 5.0 ppm. Control samples of milk and cream were spiked with each analyte at 0.01 and 0.1 ppm. Recoveries of tepraloxydim from each matrix were between 70 and 120%, with the exception of two recoveries from milk at the 0.01 ppm (68%) and 0.1 ppm (134%) spiking levels. Recoveries of 5-OH-DP and DL from liver, milk and cream were typically <70%; marginally adequate recoveries of 5-OH-DP and DL were obtained from liver at the 0.05 ppm spiking level. Recoveries generated during method development reflect a similar method performance with respect to these analytes. The petitioner indicated that low recoveries may be explained by losses during derivatization and the lengthy clean-up. Method 389/0 was proposed as the enforcement method for animals. An interlaboratory validation study was submitted for Method Nos. 389/0 (milk) and 975/1 (kidney) that showed reproducibility of the enforcement method.

Method 780 is a common moiety method for poultry that is similar to Method 975/1. Tepraloxydim and related metabolites, 5-OH-DP and similar 5-OH-metabolites, and DL-type metabolites are converted by oxidation to three common moieties (GP, OH-GP and GL acids) that are subsequently methylated and quantified as DMP, OH-DMP and DML. According to this method, tepraloxydim residues in tissues and eggs from poultry are extracted with distilled water and MeOH. $Ca(OH)_2$ is used to precipitate impurities and MeOH is removed. The remaining solution is diluted with isopropanol and water. Residues are then oxidized using alkaline H_2O_2 under reflux to convert tepraloxydim residues to GP, OH-GP and GL acids. Residues are then concentrated to dryness and redissolved in MeOH, methylated in an acidified MeOH solution to DMP, OH-DMP and DML. The solution is cleaned up on silica and C_{18} SPE columns, and residues are analyzed using GC/MS with select ion monitoring (m/z 182 for DMP; 175 for OH-DMP; 99 for DML) and expressed as equivalent parent using molecular weight conversion factors. The method LOQ is 0.05 ppm for each analyte, for a total of 0.15 ppm for DMP, OH-DMP and DML. Data for samples of eggs, muscle, liver, fat and skin that were spiked with tepraloxydim, 5-OH-DP and DL each at 0.05–5.0 ppm showed recoveries

that ranged from 70 to 126% for all three analytes (only one sample of liver spiked with 5-OH-DP was outside of the 70–120% acceptable range).

Method 975/1 was developed for bovine tissue (except liver) and is essentially the same as Method 780, except for some minor differences in the final clean-up. The reported LOQ was 0.15 ppm (0.05 ppm for each analyte). For method validation, control samples of muscle, kidney and fat were spiked with tepraloxydim, 5-OH-DP and DL each at 0.05 or 0.5 ppm. Recoveries of tepraloxydim were 70–102% from each matrix. Recoveries of 5-OH-DP were low from each matrix, with the exception of fat spiked at 0.5 ppm (80–85%). Recoveries were 54–68% for muscle spiked at 0.05 ppm. Average recoveries of DL were 62–68% from each matrix with the exception of kidney spiked at 0.05 ppm (57–89%; $\bar{x}$=71±13%).

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

Absorption, distribution, metabolism and excretion—tepraloxydim and 5-OH-tepraloxydim

In pharmacokinetics/metabolism studies in male and female rats, tepraloxydim was readily and almost completely absorbed after oral and intravenous (IV) administration. The peak plasma levels were attained within 0.5 to 2 h of dosing. The plasma half-life of radiolabelled tepraloxydim is 4 to 10 h. Excretion was rapid, mainly via the urine (65–80%), while fecal elimination comprised 16–25% of the administered dose (AD). Total recovery was 94–101% within 48 h. Excretion was two to three fold higher in the bile than the feces, suggesting enterohepatic recirculation. No accumulation of radioactivity was observed in any tissue at 120 h postdosing. The biotransformation of tepraloxydim in rats resulted in a large number of metabolites in urine, feces and bile. The main metabolic pathway was the oxidation at the pyran ring to the lactone via a hydroxy metabolite, and cleavage of the oxime ether group with the imine and oxazol as products. At near plasma T_{max} (1 h postdosing), the parent compound was the main product in the plasma, liver and kidneys. As well, the parent compound constituted 16–34% of the urinary residues, 1–2% of the fecal residue and 8–11% of the residues in the bile. The results indicate that absorption, distribution, metabolism and excretion of tepraloxydim are independent from dose levels, route of administration and sex.

Metabolism of 5-OH-tepraloxydim in male and female Wistar rats indicated that absorption was rapid and virtually complete. Radioactivity was distributed in all tissues and organs throughout the body, but by 120 h, tissue radioactivity was below 1 ppm, indicating low tissue accumulation. Excretion of orally and intravenously administered radioactivity was rapid and was mainly via the urine, accounting for 66–82% AD, while fecal excretion of radioactivity accounted for 18–29% AD. Biliary excretion amounted to about 20–26% AD. No radioactivity was detected in exhaled air. Total recovery was 93.3–100% within 48 h. Plasma clearance kinetics revealed peak whole blood and plasma concentration at 0.5–2.0 h regardless of the dose. There was no biologically relevant

gender-related or dose-related differences in absorption, distribution, metabolism and excretion of 5-OH-tepraloxydim. Identification of metabolites was not investigated in this study. The information was available in a separate study, but the report was not submitted to the PMRA for evaluation.

Acute toxicity—technical grade tepraloxydim
Technical grade tepraloxydim, ~95% purity, was of low acute toxicity in rats following oral, dermal, or inhalation exposure (oral LD_{50} >2000 mg/kg bw; dermal LD_{50} >2000 mg/kg bw; inhalation LC_{50} >5 mg/L). It was non-irritating or minimally irritating to the rabbit skin and eye. Skin sensitization testing with guinea pigs, using the maximization method, showed that tepraloxydim was not a dermal sensitizer.

Acute oral toxicity data are available for 5-OH-tepraloxydim. The oral study in rats indicated that the plant metabolite was of low acute oral toxicity.

Acute toxicity—Equinox EC herbicide
Equinox EC herbicide, containing 20.5% tepraloxydim, was considered to be of low acute toxicity by the oral, dermal and inhalation routes in rats (oral LD_{50} >2 g/kg bw; dermal LD_{50} >4 g/kg bw; LC_{50} >5 mg/L). The formulation was moderately irritating to the rabbit eye and skin. Results of skin sensitization testing in guinea pigs, based on the Buehler method, showed that the formulation was not a skin sensitizer. Based on the acute toxicity, the hazard signal words "**WARNING—EYE AND SKIN IRRITANT**" should be displayed on the product labels.

Acute toxicity—Dash HC adjuvant
Dash HC adjuvant was considered to be of low acute toxicity by the oral, dermal and inhalation routes in rats (oral and dermal LD_{50} >2 g/kg bw; LC_{50} >5 mg/L). The adjuvant was moderately irritating to the rabbit eye and skin. Results of skin sensitization testing in guinea pigs, based on the maximization method, showed that the adjuvant was not a skin sensitizer. Based on the acute toxicity, the hazard signal words "**WARNING—EYE AND SKIN IRRITANT**" should be displayed on the product labels.

Acute toxicity—Equinox EC herbicide + Dash HC adjuvant
In actual use, Equinox EC herbicide is to be mixed with Dash HC adjuvant. Acute toxicity data were generated with the mixture of Equinox EC herbicide and Dash HC adjuvant (1:4 ratio). The herbicide/adjuvant mixture was considered to be of low acute toxicity by the oral, dermal and inhalation routes in rats (oral LD_{50} >5 g/kg bw; dermal LD_{50} >4 g/kg bw; LC_{50} >5 mg/L). The mixture was moderately irritating to the rabbit eye and skin. Results of skin sensitization testing in guinea pigs, based on the Buehler method, showed that the mixture was not a skin sensitizer.

Short-term toxicity—technical grade tepraloxydim and 5-OH-tepraloxydim
Short-term toxicity data of tepraloxydim are available in the mouse (28-day and 90-day dietary), rat (28-day and 90-day dietary and 28-day dermal) and dog (30-day, 90-day and 1-year dietary).

Short-term toxicity studies in the mouse following dietary exposure to tepraloxydim indicated that the main target organ was the liver (altered cellular foci, centrilobular hypertrophy). Consistent adverse effects at high dose levels were on food consumption, body weight and body-weight gain. Other treatment-related findings also occurred at higher dose levels; the effects, not very consistent across studies, included higher serum bilirubin level, slight fatty change of the proximal tubular cells and/or myocardial vacuolization. The no observed adverse effect levels (NOAEL) established in the 28- and 90-day studies were 506 (males) and 664 (females), and 310 (males) and 424 (females) mg/kg bw/d, respectively.

Short-term toxicity studies of tepraloxydim in rats following dietary exposure indicated that the target organs were the liver (centrilobular hepatocyte hypertrophy and altered foci) and possibly kidneys (hyaline droplet degeneration). The higher serum levels of bilirubin and creatinine might be related to kidney pathology. The NOAELs established were 46 (males) and 49 (females) mg/kg bw/d in the 28-day study, and 22 (males) and 26 (females) mg/kg bw/d in the 90-day study.

Repeat dermal exposure to tepraloxydim for 28 days did not result in systemic toxicity in the rat, nor were localized reactions induced. The NOAEL for short-term dermal toxicity in the rat was 1000 mg/kg bw/d.

Short-term (4-week, 90-day and 1-year) toxicity studies in the dog following dietary exposure to tepraloxydim indicated that high levels caused general systemic toxicity with pathology of the liver and other organs, including the spleen, thyroid, urinary bladder, testes and epididymides. Several hematological and clinical chemistry parameters affected might be related to impaired nutritional status, as well as impaired lipid, protein and carbohydrate metabolism. Because of the small group size (2/sex) and the highly variable values of the many parameters examined, the findings in the 4-week study were inconclusive and no NOAEL or lowest observed adverse effect level (LOAEL) could be established. For the 90-day study, the LOAEL and NOAEL were 10 000 (358 (male), 325 (female) mg/kg bw/d) and 2000 ppm (68 (male), 63 (female) mg/kg bw/d), respectively. For the 1-year studies, the LOAEL and NOAEL were 2000 (56.0 (male), 60.6 (female) mg/kg bw/d) and 400 ppm (11.5 (male), 12.5 (female) mg/kg bw/d), respectively.

Long-term toxicity/oncogenicity—technical grade tepraloxydim

Long-term dietary toxicity and/or oncogenicity studies of tepraloxydim were conducted in the mouse (18-month) and rat (24-month). In the mouse study that assessed oncogenic potential of tepraloxydim, the NOAEL for systemic toxicity in male mice was 37 mg/kg bw/d; however, a NOAEL for systemic toxicity was not established in females because of the adverse body weight effect at the lowest dose level of 52 mg/kg bw/d. A higher number of palpable masses in the abdominal region was observed in high-dose females (28 versus 17 of control). The incidence of hepatocellular tumours was increased in high-dose mice (3 adenoma versus 0 in control males; 3 adenomas and 3 carcinomas versus 0 in control females). The incidence of liver tumours in high-dose females exceeded the historical control incidences (0-1/50 based on 10 studies). The high dose level tested exceeded the maximum tolerated dose (MTD). It was concluded that there was evidence that tepraloxydim induced liver tumours in female mice. However, the exceedingly high dose tested that resulted in the induction of liver tumours in the female mice is not biologically relevant for carcinogenicity risk assessment in humans.

In the rat, the NOAELs established were 5 (males) and 38 (females) mg/kg bw/d. The incidence of liver tumours was higher in high-dose males (chronic study) and females (oncogenicity study). The incidence of tumours in adrenal medulla was higher in high-dose rats. When the incidence of these tumours in the two studies were combined and comparison was made with the concurrent and historical control values, it became apparent that the incidence of liver tumours was higher in both high-dose male and female rats as well as in mid-dose males, but was within the range of historical control values. For tumours in the adrenal medulla, there was no clear evidence of significantly higher incidence in rats exposed to tepraloxydim when compared with the concurrent control incidence. However, the incidence of the adrenal medulla tumour observed in these two studies was unusually high when compared to historical control values. It was concluded that there was insufficient evidence that the test substance induced tumours in male and female rats.

Several non-guideline mechanistic studies designed to investigate a relationship of tepraloxydim exposure and tumour induction in the liver of rats were available. In these studies, rats were exposed to tepraloxydim via the diet for periods of up to 13 weeks and their livers were processed for various biochemical, immunological and histopathological examinations. The reports of these studies were deficient in the following : lack of detail, lack of proper control groups, highly variable findings. Nonetheless, the findings of these supplementary studies indicated that tepraloxydim did not initiate the formation of preneoplastic lesions in the liver, but, like phenobarbital, promoted the development of the lesions. There was some evidence of heightened activity and increased DNA synthesis in hepatocytes of rats exposed to tepraloxydim. In addition, a study was designed to compare serum bilirubin and creatinine levels using the standard colorimetric method and an enzymatic method. The purpose of this study was to provide evidence to support that the higher serum bilirubin and creatinine levels in the rat studies were not related to tepraloxydim exposure; the higher levels were in fact due to the inherent weakness of the colorimetric method used in rat studies. The data derived from the enzymatic (creatinine

and bilirubin) and HPLC (bilirubin) methods cannot be accepted due to the lack of historical control data.

Results of mechanistic studies demonstrated that tepraloxydim was not an initiator for the development of preneoplastic lesions in the liver of rats. However, at high dose levels, tepraloxydim might promote the development of these lesions that were initiated by a hepatocarcinogen.

Genotoxicity—technical grade tepraloxydim and 5-OH-tepraloxydim
The mutagenic potential of tepraloxydim and 5-OH-tepraloxydim was assessed in a battery of in vitro and in vivo genotoxicity tests assessing gene mutation, chromosome aberration and DNA damage/repair in microbial and mammalian systems. The results were largely negative. The only slightly positive findings were observed with 5-OH-tepraloxydim in an in vitro unscheduled DNA synthesis (UDS) in primary rat hepatocytes when the values were assessed on the basis of percentages of cells in repair. When the UDS assay was repeated with 5-OH-tepraloxydim orally administered to male rats, i.e., in an in vivo assay, there was no increase in UDS in bone marrow cells. The slightly positive findings observed in the in vitro UDS assay were unlikely to be toxicologically relevant, especially when the in vivo UDS assay gave negative results.

Reproductive toxicity and teratogenicity—technical grade tepraloxydim and 5-OH-tepraloxydim
Reproductive toxicity data available in the rat indicated that tepraloxydim did not affect reproductive performance or other reproductive parameters. At a maternally toxic dose (body weight impairment), tepraloxydim caused development delays in the offspring. The NOAEL and LOAEL for both maternal and reproductive/offspring toxicity were 500 ppm (50.9 (males) and 54.7 (females) mg/kg bw/d) and 2500 ppm (253 (males) and 274 (females) mg/kg bw/d), respectively.

The teratogenic potential of tepraloxydim was assessed in the rat and rabbit. In the rat (two related studies), the LOAEL and NOAEL for maternal toxicity were 360 and 120 mg/kg bw/d, respectively, based on effects on food intake and body weight. At ≥120 mg/kg bw/d, fetotoxicity was observed (marginally lower fetal weight, skeletal retardation and statistically significantly higher incidence of hydroureter). Thus, offspring toxicity occurred at a maternally non-toxic dose, indicating higher sensitivity of the offspring to the toxicity of tepraloxydim. The LOAEL and NOAEL for fetotoxicity were 120 and 40 mg/kg bw/d. At 360 mg/kg bw/d, there were three fetuses from two litters with dilation of both ventricles and two fetuses from two litters with filiform tails, which corresponded to absent caudal and sacral vertebrae. Because these findings were rare occurrences in rats and did not occur in current and historical controls, these malformations were considered treatment-related. Based on these malformations, the LOAEL and NOAEL for teratogenicity were 360 and 120 mg/kg bw/d.

The rabbit data did not demonstrate teratogenicity or developmental toxicity at maternally toxic doses. The LOAEL and NOAEL for maternal toxicity were 180 and 60 mg/kg bw/d, respectively, based on body-weight effect. The NOAEL for developmental toxicity was 180 mg/kg bw/d, the highest dose tested.

The teratogenic potential of 5-OH-tepraloxydim was also assessed in the rat. The data did not demonstrate teratogenicity or developmental toxicity at maternally toxic doses. The LOAEL and NOAEL for maternal toxicity were 360 and 120 mg/kg bw/d, respectively, based on body-weight effect. The NOAEL for developmental toxicity was 360 mg/kg bw/d, the highest dose tested.

Neurotoxicity—technical grade tepraloxydim
Acute and short-term 90-day neurotoxicity tests in rats did not provide definitive evidence for the neurotoxicity potential of tepraloxydim. The highest doses tested were 2000 mg/kg bw and 428 mg/kg bw/d in the acute and 90-day studies, respectively.

Special toxicity endpoints
From the available data, there is no evidence to suggest that tepraloxydim might be a toxicant on the endocrine or immune systems.

Adequacy of toxicological database
The toxicological database for tepraloxydim is complete and adequate.

3.2 Determination of acceptable daily intake (ADI)

In choosing the most appropriate NOAEL for the ADI determination, the following results were considered. Short- and long-term toxicity studies in mice, rats and dogs demonstrated that the female animal was slightly less sensitive than the male to the toxicity of tepraloxydim. Although no NOAEL was established for females in the 18-month mouse oncogenicity study, the NOAEL for female mice is estimated to be slightly higher than 37 mg/kg bw/d established for males.

Comparing the NOAELs established in similar 90-day dietary toxicity testing of tepraloxydim in the mouse, rat and the dog, the rat appears to be the more sensitive species. The lowest short-term toxicity NOAELs were established in the rat study (22 (males) and 26 (females) compared to 310 (males) and 424 (females) in the mouse, and 63 (males), 68 (females) in the dog).

A NOAEL of 5 mg/kg bw/d was established in male rats in the two-year oncogenicity study based on reduced food consumption, reduced body weight and liver pathology. Using this NOAEL, the standard uncertainty factors (UF) of 100 and a safety factor of ×3 for the higher sensitivity of offspring observed in the rat teratology study (lower pup weight, delayed development and hydroureter at a maternally non-toxic dose), an ADI of 0.02 mg/kg bw was established.

This ADI provides the following margins of safety (MOS):

- malformation (dilation of heart ventricle and filiform tail) in rat fetuses, NOAEL of 120 mg/kg bw/d for this endpoint: MOS = 6000
- developmental toxicity in rats (lower pup weight, delayed development and hydroureter at a maternally non-toxic dose), NOAEL of 40 mg/kg bw/d for this endpoint: MOS = 2000

3.3 Acute reference dose (ARfD)

Technical grade tepraloxydim is of low acute toxicity; therefore, no ARfD is needed for the general population.

Given the teratogenic concerns observed in the rat teratology study, an ARfD of 0.13 mg/kg bw is determined for women of child-bearing age (13–50 years of age), based on the developmental NOAEL of 40 mg/kg bw/d, a standard UF of 100 and a safety factor of ×3 for offspring toxicity at a maternally non-toxic dose.

3.4 Toxicological endpoint selection—occupational and bystander risk assessment

Farmers, custom applicators and re-entry workers have potential for short- to intermediate-term exposure to Equinox EC herbicide via the dermal and inhalation routes. For short- and intermediate-term occupational exposures via the dermal and inhalation routes, the NOAEL of 40 mg/kg bw/d from the rat teratology study was selected. Offspring toxicity, including decreased pup weights and increased skeletal retardation, was observed at maternally non-toxic doses. A safety factor of ×3 is added to account for higher sensitivity of the offspring. The target MOE is 300.

Since an appropriate endpoint for the dermal risk assessment of tepraloxydim was selected from an oral study, an estimate of dermal absorption is required. A default dermal absorption rate of 100% was used in the risk assessment as the quantitative dermal absorption value could not be obtained from the submitted dermal penetration study. The dermal penetration study had several limitations and inconsistencies in the results. A 10 cm^2 skin area of nine groups (four animals per group) of Wistar rats was treated with nominal 0.005, 0.05 and 0.5 mg/cm^2 doses of 14C-BAS 620 H (isomer of tepraloxydim) in 100 µL Solvesso 200 solution and monitored up to 72 h postdosing. At the end of the 8 h exposure period, a skin wash was performed after removing the protective dressings and the groups were sacrificed at 8, 24 and 72 h. The majority of the administered dose was recovered from the protective dressings in all groups with high variability (16–92%). The amount recovered in protective dressings is not considered available for absorption. When dermal absorption was recalculated based on the available dose, the highest rate was observed in 8 h groups for all doses (73–110%). This higher recovery in the 8 h groups is not due to peak dermal absorption at 8 h, as the amount recovered at the application site decreased over 24 and 72 h, which corresponded with increased radioactivity in urine and feces. In addition, the doses used in the study do not fit the

exposure scenario of the expected doses in the field. Based on all the limitations of the study, a dermal absorption value could not be determined and the study was rejected.

3.5 Impact on human and animal health arising from exposure to the active substance or to its impurities

3.5.1 Occupational exposure and risk

3.5.1.1 Handler exposure and risk

Equinox EC is an emulsifiable concentrate formulation of tepraloxydim (200 g a.i. per litre) proposed for use as a postemergent herbicide on lentils, dry peas and flax crops in western Canada. Equinox EC is required to be used with the proposed adjuvant Dash HC. The maximum rate of application is 50 g a.i./ha. The proposed application would be by ground, using standard ground boom equipment. Farmers and custom applicators would mix, load and apply the product to all crops. The average Canadian farm size for these crops is 70–120 ha. Typical hectarages of cereal crops treated per day by ground boom equipment are 100 ha for farmers and up to 300 ha for custom applicators. As Equinox EC would be applied only once, early in the growing season, farmers would typically be exposed from one to five days (short-term) and custom applicators could be exposed intermittently over a short to intermediate term.

Handlers (mixers, loaders and applicators) have potential for exposure to Equinox EC herbicide during application to flax, lentil and dry pea crops. The exposure was calculated by using unit exposure (dermal and inhalation) data from the Pesticide Handlers Exposure Database (PHED). The PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates. With a few exceptions, the PHED estimates meet the criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides.

Appropriate subsets of A or B grade data, based on the best-fit measure of data distribution, liquid open mixing/loading and ground boom applicator (open cab) files of PHED were selected for each use scenario of Equinox EC herbicide. The data contained in these selected files were generated with a single layer of clothing and gloves as protective equipment, with the exception of the ground boom applicator, for which exposure was estimated for applicators not wearing gloves. All data were normalized for kilogram of active ingredient handled.

Total dermal and inhalation exposure estimates for farmers, assuming 100 ha area treated per day, and for custom applicators assuming, 300 ha area treated per day, at the maximum application rate of 50 g a.i./ha were combined to obtain total systemic exposure in milligram per kilogram body weight per day. The NOAEL of 40 mg/kg bw/day from the rat oral developmental toxicity study was considered most appropriate for short- to intermediate-term exposure scenario of Equinox EC to obtain margins of exposure (MOEs). Considering sensitivity of the young noted in rat development study, the target MOE of 300 would be an acceptable risk from exposure to tepraloxydim. All MOEs exceed the target of 300 and are considered acceptable. Acute eye and skin irritation effects will be mitigated through the use of goggles and gloves during mixing and loading. Results are presented in Table 3.5.1.1.1.

Table 3.5.1.1.1 Mixer/loader/applicator exposure estimates and risk assessment for Equinox EC herbicide

Occupational scenario	Systemic exposure[1] (mg/kg bw/day)	Margin of exposure (MOE)[2]
Farmers	0.00618	6470
Custom Applicators	0.01855	2160

1 Systemic exposure (mg/kg bw/day) = PHED unit exposure (dermal + inhalation) × application rate × area treated per day × 1/1000 (mg/µg) ÷ 70 kg bw

2 MOE = NOAEL (40 mg/kg bw/day) ÷ systemic exposure

3.5.1.2 Postapplication exposure and risk

There is a potential for postapplication dermal exposure to workers re-entering treated fields to assess herbicide efficacy, scout and irrigate. Growers, hired workers or professional scouters would generally perform scouting throughout the season for two to three hours per visit to the field. Professional scouters may visit several fields in a day. Irrigation is required for lentils and dry peas, but not for flax, which is grown on black soil that does not require irrigation. There is postapplication exposure for irrigation workers while handling water hoses in the field and exposure is similar to scouting. For lentil and peas crops, some hand weeding is also performed; however, exposure from this activity is low. Negligible exposure is expected from swathing and harvesting as these activities are done mechanically and the proposed preharvest interval is 60 days. Based on the above noted postapplication exposure scenario, re-entry workers could be exposed for a short-term duration throughout the growing season up to 8 hours per day. The primary route of exposure for re-entry workers is dermal through contact with foliar residues. Inhalation exposure is expected to be negligible as postapplication activities would normally be performed several days after spraying when residues are dry and the vapour pressure of tepraloxydim is very low at 2.7×10^{-7} hPa at 25°C.

Dermal exposure to workers re-entering treated areas is calculated by coupling crop-specific dislodgeable foliar residue (DFR) values with activity-specific transfer coefficients (TCs) based on data from the Agricultural Re-entry Task Force (ARTF), of which the registrant is a member. The estimated exposure estimates were combined with the NOAEL of 40 mg/kg bw/day from the oral rat developmental toxicity study to obtain MOEs. All MOEs are above the target of 300 and acceptable. Exposure estimates and MOEs are presented in Table 3.5.1.2.1.

Table 3.5.1.2.1 Re-entry exposure and risk estimates for Equinox EC herbicide

Crop	Re-entry activity	Transfer coefficient[1] (cm^2/h)	DFR[2] ($\mu g/cm^2$)	Exposure[3] mg/kg bw/day	MOE = NOAEL ÷ EXPOSURE
Flax, lentil, dry peas	scouting irrigation	1 500	0.1	0.01714	2 340
Lentil, dry peas	hand weeding	100	0.1	0.00114	35 090

1 TC: transfer coefficients, expressed in cm^2/h, are based on the surface area of a 70 kg person.

2 DFR: standard default value of 20% of the application rate being dislodged on the day of application was used.

3 Exposure (mg/kg bw/day) = DFR × TC × work day duration × dermal absorption/body weight, where 8 hours/day duration is considered to be the typical work day; 100%, the dermal absorption rate; and 70 kg, the body weight.

3.5.2 Residential exposure and risk

Given that the products are not domestic products, a residential exposure assessment was not required.

3.5.3 Bystander exposure and risk

For the proposed agricultural use scenario, bystander exposure during and after application was considered to be negligible. The following statement is required on the label to reduce bystander exposure: "Apply only when the potential for drift to areas of human activity such as houses, cottages, school and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings."

4.0 Residues

4.1 Residue summary

Nature of the residue in plants
Tepraloxydim (radiolabelled in either the pyran or the cyclohexene ring positions) was applied to soybeans as a postemergent application 51 days after seeding at a rate of 100–300 g a.i./ha. The predominant residue was 5-OH-DP and it was found in soybean seed (16.06% total radioactive residue (TRR), 0.258 ppm) 60 days after treatment (DAT). The proposed metabolic pathway for tepraloxydim in/on soybeans is shown in Figure 4.1.1.

Metabolism in the two labelled studies involving soybeans was similar, except that in the cyclohexene-labelled study, DD was found at 5.88% of the TRR (0.094 ppm) and in the pyran-labelled study it was found at 16.0% TRR (0.233 ppm). Although not reviewed by the PMRA, the soybean field trials reviewed by the United States Environmental Protection Agency (USEPA) showed that DD is present at roughly 3–7% of the combined residues of tepraloxydim and 5-OH-DP. On this basis, the USEPA concluded that DD need not be included in the U.S. tolerance expression for soybeans. Since soybeans belong to the same crop group (legume vegetables) as lentils and dry peas, it is not likely that DD is a major metabolite in these crops (lentils and dry peas were not specifically analyzed for DD in the Canadian field trials). Furthermore, for the Canadian field trials for lentils and dry peas that were conducted at the maximum label rate, residues of tepraloxydim, 5-OH-DP and metabolites convertible to DMP and OH-DMP were below the LOQ. **Therefore, for the present use pattern of tepraloxydim, Canada will not include the DD metabolite in the ROC for lentils and dry peas. However, this decision would be re-evaluated if there were a future expansion of use that resulted in measurable residues in lentils, dry peas or any other legume vegetable crop.**

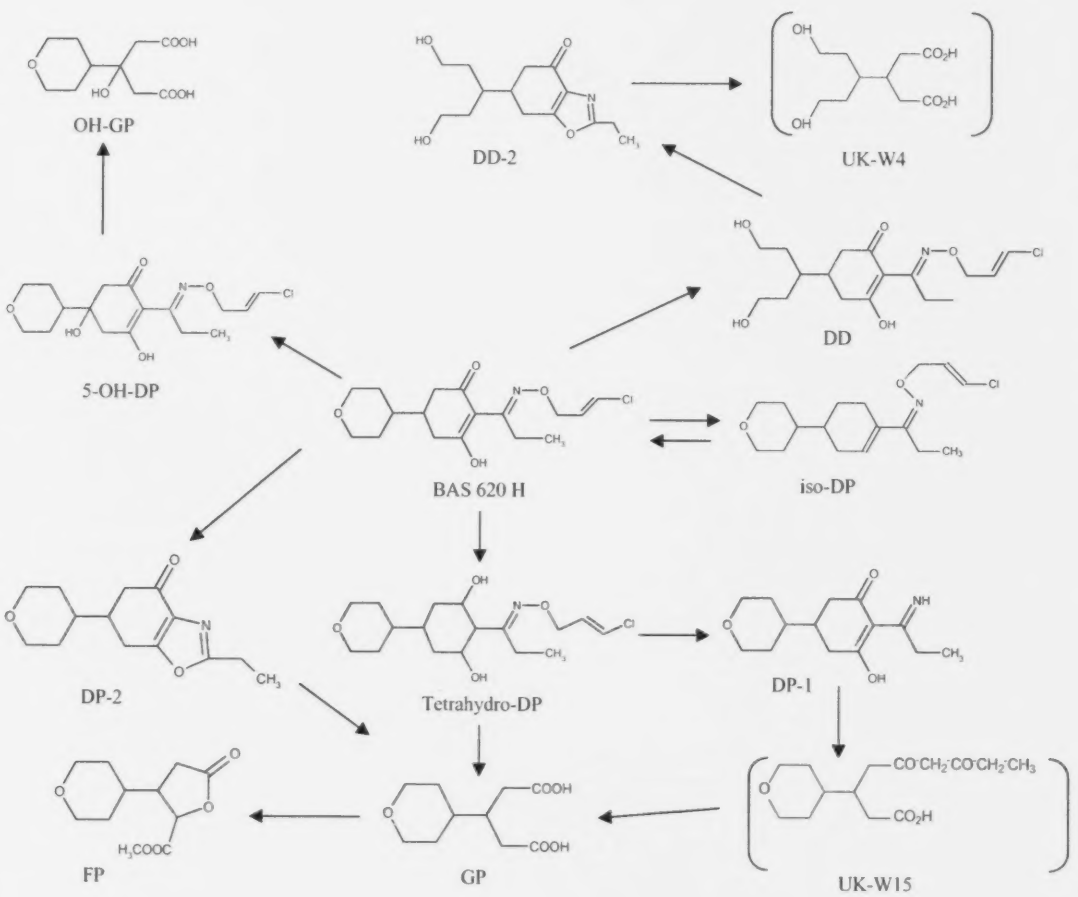
There were no major differences between the metabolic profiles in the tepraloxydim metabolism studies for the pyran and cyclohexene-labelled structures in/on soybeans. Therefore, metabolism studies involving tepraloxydim labelled in the cyclohexene position are sufficient for other plant commodities.

For metabolism in/on canola, tepraloxydim (cyclohexene-labelled) was applied at the 6- to 8-leaf stage of growth at 100–300 g a.i./ha. Results show that tepraloxydim is not present in seed, and that 5-OH-DP, 5-OH-DP-1 and GP were the major metabolites (12–37% TRR). The DD metabolite was not detected in canola seed, and was a minor metabolite in canola straw (3.8% TRR, 0.062 ppm). The proposed metabolic pathway for tepraloxydim in/on canola is shown in Figure 4.1.2.

The metabolism study for tepraloxydim in/on sugar beets was not accepted since a considerable proportion of the residues (24.9–49.2% of the TRR 45-123 DAT) were not identified/characterized.

Therefore, metabolism in three diverse crops has not been demonstrated, and the metabolism of tepraloxydim in soybeans and canola is qualitatively and quantitatively different. However, the metabolism of tepraloxydim in/on canola can be extended to crops within the oilseed group (Crop Group 20) and metabolism of tepraloxydim in/on soybeans can be extended to other crops within the legume vegetable crop group (Crop Group 6).

Figure 4.1.1 Proposed metabolic pathway of tepraloxydim in/on soybeans
(Structures in parenthesis are not proven)

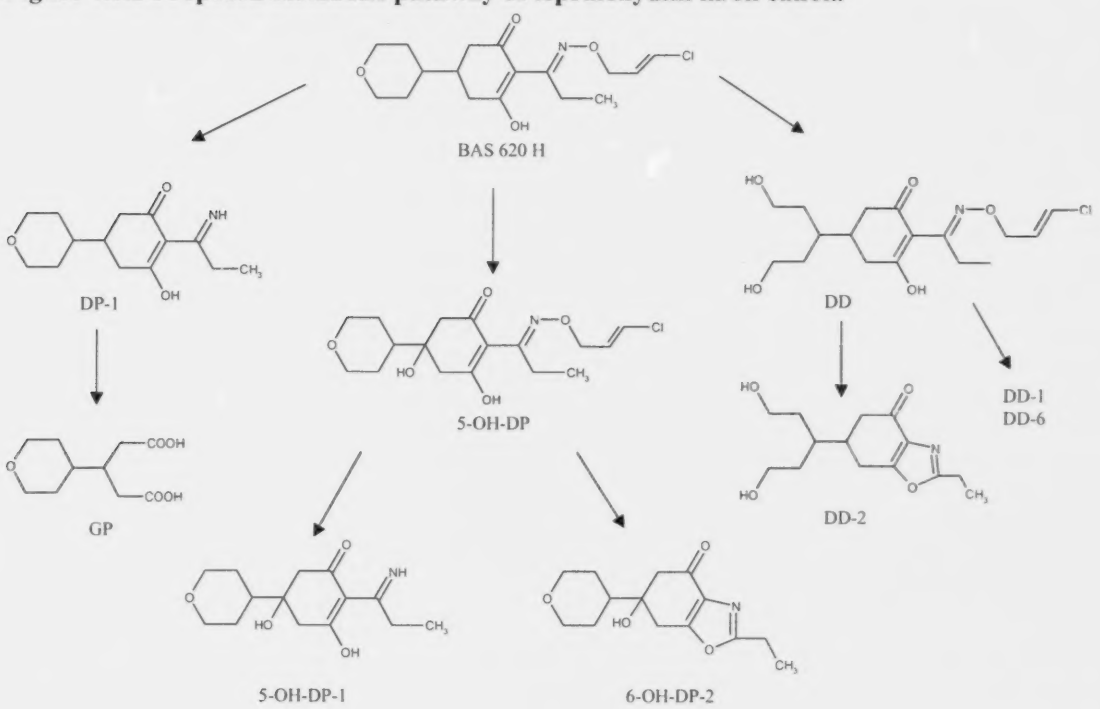


On the basis of the metabolism of tepraloxydim in/on soybean and canola, the ROC is defined as the combined residues of tepraloxydim and metabolites convertible to GP and OH-GP.

Confined accumulation in rotational crops

Tepraloxydim (labelled either in the cyclohexene or pyran positions) was applied to soil at 112 g a.i./ha. Chard, radish and sorghum were planted 40 DAT, chard and radish were planted 167 DAT, and wheat was planted 187 DAT. Only radish tops planted 40 DAT contained radioactive residues (0.022–0.037 ppm) that exceeded 0.01 ppm. The only residue identified was DP-2 (<0.001 ppm). GP was tentatively identified by the presence of its methyl ester (DMP). Since the soil metabolism study shows that the parent compound was only present at 1.8–7.8% TRR 30 DAT and that no major metabolites were detected, it is not expected that tepraloxydim and its related metabolites would be present for uptake by the plant 40 DAT (the shortest time interval tested). On this basis, a plant back interval of 40 days for all rotational crops is required.

Figure 4.1.2 Proposed metabolic pathway of tepraloxydim in/on canola



Nature of the residue in animals

Tepraloxydim

Tepraloxydim (both cyclohexene and pyran ring-labelled structures) was administered in the diet to lactating goats at 0.33 and 7.43 mg/kg/day for [cyclohexene-4(6)-C^{14}]tepraloxydim, and at 0.47 and 11.1 mg/kg bw/day for [pyran-4-C^{14}]tepraloxydim. The predominant residues in the various matrices from the cyclohexene-4(6)-^{14}C labelled study were, expressed as % TRR, tepraloxydim (30.9% in milk, 9.7% in liver, 30.7% in kidney, 61% in muscle, 71.8% in fat), DL (19.5% in milk, 4.9% in liver, 7.4% in kidney, 5.3% in muscle) and N15 (16.5% in liver only). The proposed metabolic pathway of tepraloxydim in the goat is shown in Figure 4.1.3. None of the metabolites identified formed as a result of cleavage of the bond that joins the pyran and cyclohexene ring structures. Furthermore, the metabolic profile observed in the [pyran-4-^{14}C]tepraloxydim study was similar to that of the [cyclohexene-4(6)-C^{14}]tepraloxydim study. Therefore, cleavage of the bond that joins the cyclohexene and pyran rings is not evident, and metabolism studies involving [cyclohexene-4(6)-C^{14}]tepraloxydim are considered to be sufficient. Laying hens were also fed [cyclohexene-4(6)-C^{14}]tepraloxydim at 0.7 and 15.4 mg/kg bw/d in the diet. The predominant residues, expressed as % TRR, were tepraloxydim (23.4% in egg whites, 20.6% in liver, 14.8% in muscle, 45.6% in fat, 39.2% in skin), 2-OH-P-DP (10.3% in egg whites, 12.0% in muscle), DL (4.8% in egg whites, 5.7% in skin), DP-2 (22.1% in egg whites, 9.0% in muscle, 15.0% in fat, 17.6% in skin) and DP-6 (8.9% in egg whites, 14.6% in muscle, 9.1% in fat, 17.4% in skin). The proposed metabolic pathway of tepraloxydim in the hen is shown in Figure 4.1.4.

Figure 4.1.3 Proposed metabolic pathway of tepraloxydim in the goat
(dashed arrows indicate non-enzymatic conversion)

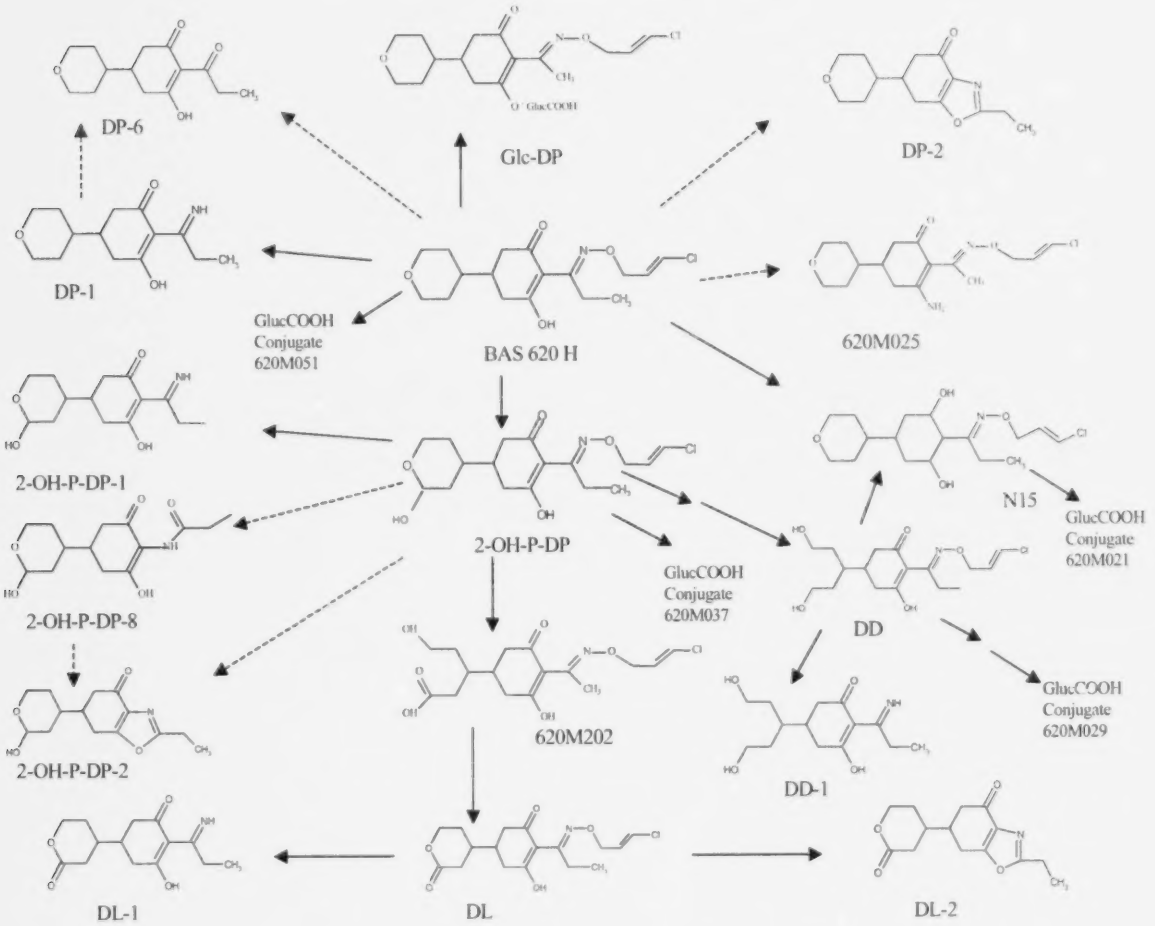
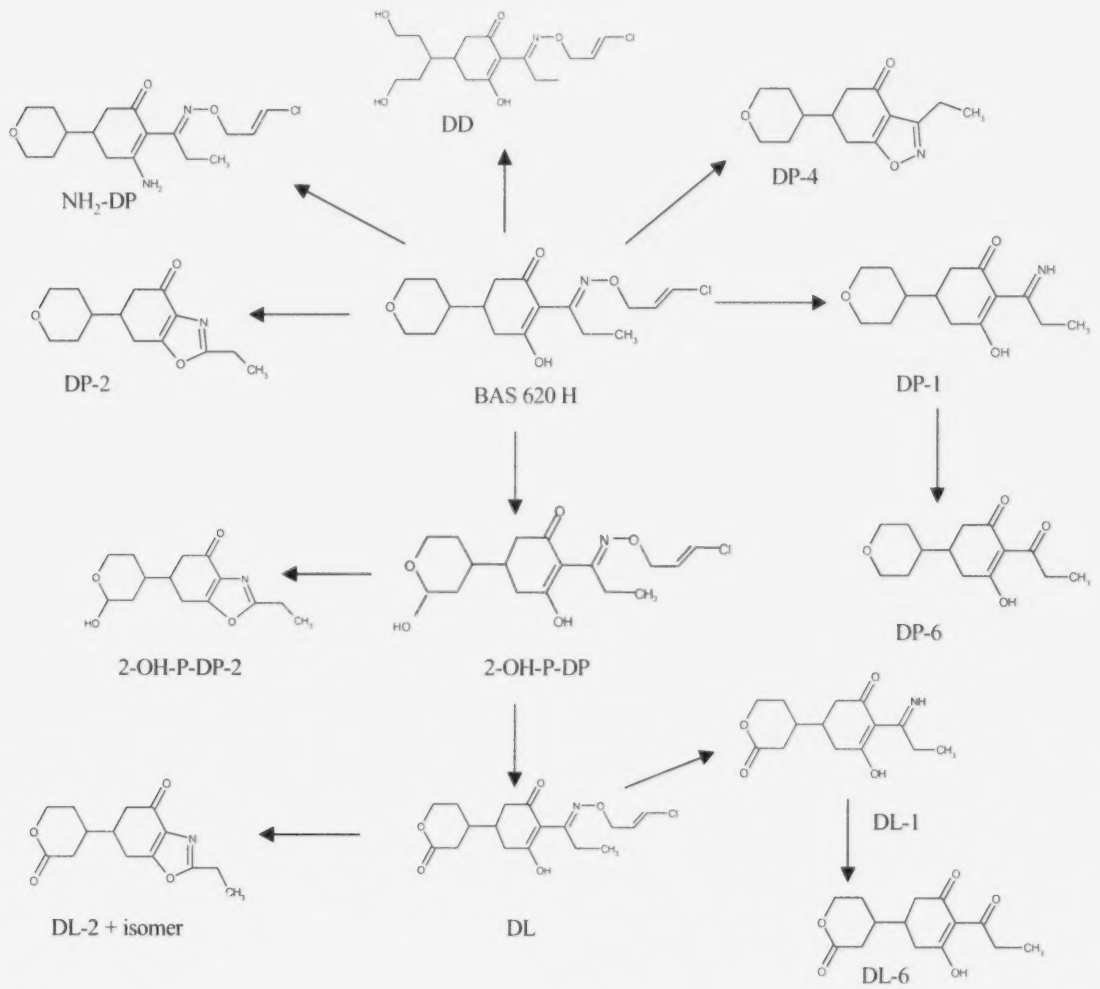


Figure 4.1.4 Proposed metabolic pathway of tepraloxydim in the hen



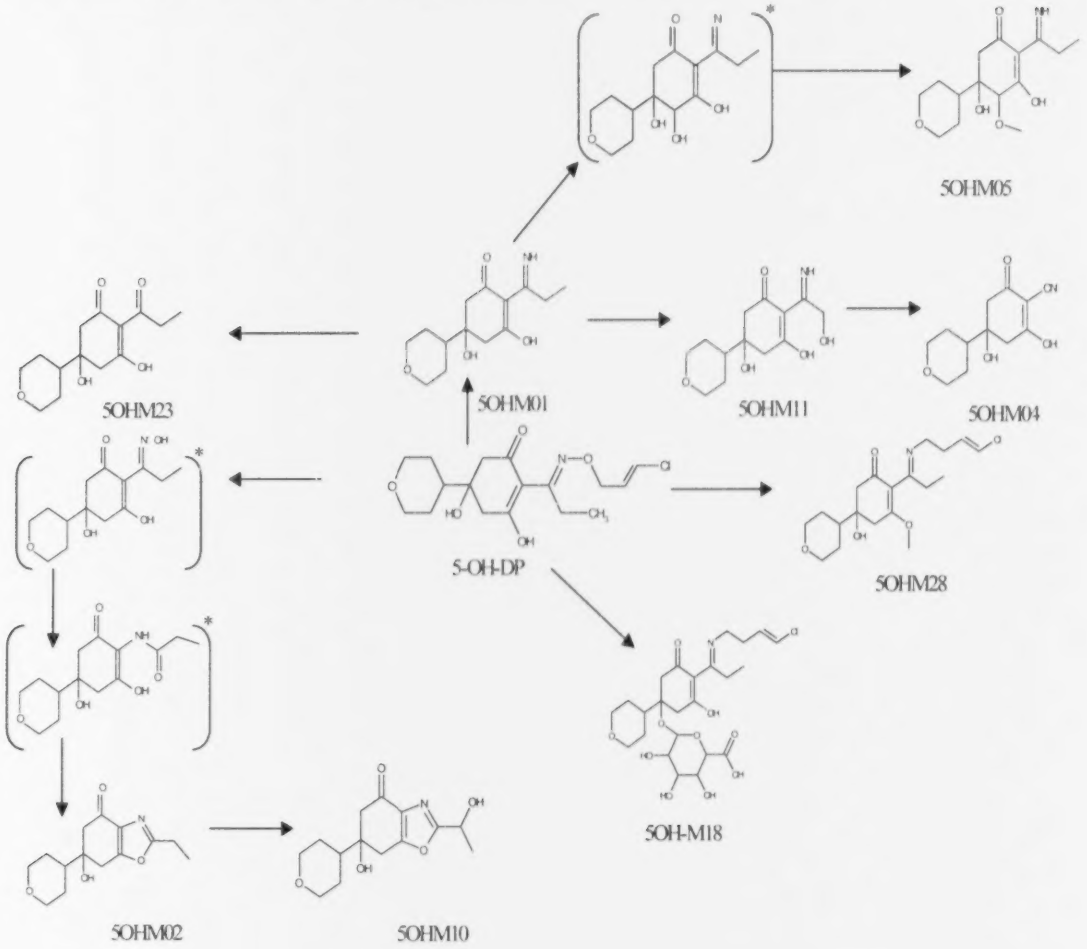
The metabolism of tepraloxydim in ruminants and poultry is similar. It primarily involves hydroxylation and oxidation of the pyran ring, dealkoxylation of the side chain and acid mediated isomerization to form an amide (Beckmann rearrangement) with subsequent ring closure to form 2-OH-P-DP. As described above, there is no evidence that the bridge between the pyran and cyclohexene rings is cleaved. In both species, tepraloxydim is the principle residue in tissue, eggs and milk, along with varying amounts of 2-OH-P-DP. Differences in the metabolic profiles between the two species are as follows. The first difference is that in goats DL accounts for 20% of the TRR in milk and up to 7% of the TRR in tissues, whereas in poultry the DL metabolite is ≤6% of the TRR for all poultry matrices. The second difference is that in goat liver the N15 metabolite accounts for 9–17% of the TRR, whereas in poultry liver N15 is absent. The third difference is that the DP-2 metabolite is a major metabolite (15–22% TRR) in egg yolks and in poultry skin and fat, but is not present in goats. However, although there were some differences, the overall conclusion is that the metabolic profile of tepraloxydim in ruminants and poultry is similar.

5-OH-DP

Based on the results of the metabolism studies involving [cyclohexene-4(6)-C^{14}]tepraloxydim and [pyran-4-C^{14}]tepraloxydim in the goat (described above), cleavage of the bond that joins the two ring structures is considered to be insignificant. Hence, the petitioner carried out additional metabolism studies with 5-OH-DP, the major plant metabolite, that were labelled in the cyclohexene position only.

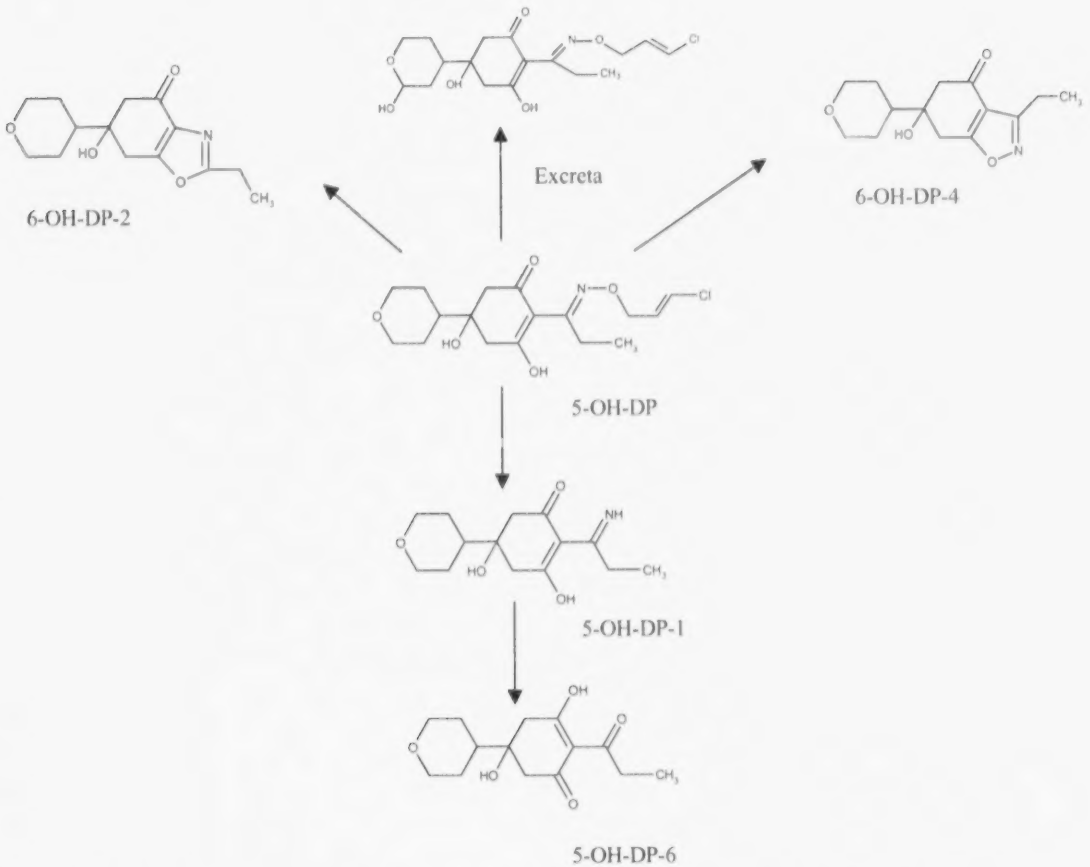
In the study involving the lactating goat, [cyclohexene-5-^{14}C]5-OH-DP was administered in the diet at 0.26 and 8.04 mg/kg bw/day. The predominant residues, expressed as % TRR, consisted of 5-OH-DP (36.0% in milk, 33.4% in kidney and 12.7% in liver), 5-OH-DP-1 (15.3% in milk, 11.3% in kidney and 7.6% in liver), 6-OH-DP-2 (8.5% in milk) and 5-OH-M10 (21.0% in milk). The proposed metabolic pathway of 5-OH-DP in the goat is shown in Figure 4.1.5. In another study, [cyclohexene-5-C^{14}]5-OH-DP was fed to laying hens at 0.68 and 17.2 mg/kg bw/day in the diet. The predominant residues, expressed as % TRR, were 5-OH-DP (76.7% in egg whites, 58.7% in egg yolks, 44.7% in liver, 64.4% in muscle, 72.2% in fat, 65.0% in skin), 5-OH-DP-2 (10.3% in egg yolks, 9.0% in muscle, 11.0% in skin) and 5-OH-DP-6 (11.5% in egg whites, 10.7% in egg yolks, 11.2% in liver). The proposed metabolic pathway of 5-OH-DP in the hen is shown in Figure 4.1.6.

Figure 4.1.5 Proposed metabolic pathway of 5-OH-DP in the goat
(structures marked by an asterix are proposed intermediates not found in tissue).



The metabolism of the major plant metabolite, 5-OH-DP, in ruminants and poultry is similar. It primarily involves dealkoxylation of the side chain to form 5-OH-DP-1 and 5-OH-DP-6, and acid mediated isomerization to form amides (Beckamnn rearrangement) with subsequent ring closure to form 6-OH-DP-2 and 6-OH-DP-4. In both species, 5-OH-DP is the principle residue in tissues, eggs and milk, along with substantial amounts of 5-OH-DP-1 and 6-OH-DP-2. Differences in the metabolic profiles between the two species are as follows. The first difference is that 5-OH-M10 is not present in poultry matrices, whereas it comprises 21% TRR in milk. The second difference is that 5-OH-DP-6 is the major metabolite in most poultry matrices (3–19%), whereas it was only detected in trace quantities in the goat liver.

Figure 4.1.6 Proposed metabolic pathway of 5-OH-DP in laying hens



Despite these small differences, the metabolism of 5-OH-DP in ruminants, poultry and the rat is essentially similar. Therefore, the ROC in animal products is defined as tepraloxydim, 5-OH-DP and metabolites that are convertible to DMP, OH-DMP and DML.

Methods for residue analysis of plants and plant products

The common moiety Method No. D9704/1 (an LC/MS/MS method) was proposed for data gathering and enforcement purposes. The method LOQ for tepraloxydim, 5-OH-DP and other metabolites convertible to GP and OH-GP was reported as 0.10 ppm (0.05 ppm for GP + 0.05 ppm for OH-GP). This method was found to give acceptable recoveries (69–124% for canola seed, 57–105% for soybean seed, 72–103% for dry pea seed and 61–102% for dry pea forage). The interlaboratory validation study supports the reliability and reproducibility of Method D9704/1 for determination of tepraloxydim residues convertible to GP and OH-GP in plants. Method No. 587, a common moiety method that is similar to D9704/1, was successfully radiovalidated using samples from the

[cyclohexene-4(6)-^{14}C]tepraloxydim soybean metabolism study. Multiresidue method testing, using the USFDA MRMs from the *Pesticide Analytical Manual* (PAM, Vol. 1, 3rd edition, 1/94), showed that tepraloxydim, 5-OH-DP, DL and GP were not efficiently recovered. Therefore, the USEPA MRMs are not applicable as enforcement methods for tepraloxydim residues.

Methods for residue analysis of food of animal origin

The common moiety Method No. 389/0 (a GC/MS method) was proposed for data gathering and enforcement purposes. The method LOQ for tepraloxydim residues convertible to DMP, OH-DMP and DML was reported as 0.15 ppm (0.05 ppm for DMP + 0.05 ppm for OH-DMP + 0.05 ppm for DML). This method was found to give recoveries that were, in general, acceptable with the following exceptions: two recoveries of tepraloxydim from milk spiked at 0.10 ppm (68%) and 0.1 ppm (134%) and recoveries of 5-OH-DP and DL from liver, milk and cream were typically <70%. However, the interlaboratory validation did support the reliability and reproducibility of Method 389/0 for the determination of DMP, OH-DMP and DML in milk and kidney matrices. The extraction efficiency indicated that residues of tepraloxydim and 5-OH-DP (convertible to DMP and OH-DMP) were recovered within acceptable limits (70–120%), but DL (convertible to DML) showed recoveries that ranged from 58–88%. Method 389/0 was successfully radiovalidated using samples from the [cyclohexene-5-^{14}C]5-OH-DP goat metabolism study.

Storage stability data

Plant

The data presented in the freezer storage stability study for rapeseed indicated that residues of tepraloxydim and 5-OH-DP were stable at –20°C for two years in rapeseed immature plant matrices, seed and straw that were spiked at 1 ppm for each analyte. The data presented in the freezer storage stability study for dry pea seed indicated that residues of tepraloxydim and 5-OH-DP were stable at –5°C for 24 months in dry pea seed spiked at 0.5 ppm for each analyte, and for 36 months for dry pea forage also spiked at 0.05 ppm for each analyte. Samples of soybean seed that were spiked individually with 0.5 ppm of tepraloxydim, DP-1, DP-2, GP and 5-OH-DP showed acceptable (70–120%) recoveries following 36 months of storage at –5°C, except for the cases of DP-2 and GP where recoveries were 65–69%.

Animals

The data presented in the freezer storage stability study indicated that residues of tepraloxydim, 5-OH-DP and DL were stable at –18°C for one year in muscle, liver, milk and eggs spiked at 0.5 ppm for each analyte.

Crop field trials

Supervised crop field trials in lentils, dry peas and flax were conducted in Canada (zones 5, 7 and 14) with tepraloxydim at 50 and 100 g a.i./ha (1 and 2× the maximum Canadian label rate) in the presence of the Dash HC adjuvant (1 L/ha). The residues in lentils, dry peas and flax collected at 60 DAT were all <0.10 ppm (LOQ), with the exception of flax seeds treated at 100 g a.i./ha (2× the maximum Canadian label rate) that showed residues that were <0.10–0.12 ppm. Consequently, maximum residue limits (MRLs) of 0.10 ppm, based on the method LOQ for plants, should be established to cover residues of tepraloxydim in lentils, dry peas and flax. Residue decline studies were not submitted. However, since residues were below the LOQ for crop trials conducted at the maximum Canadian label rate, residue decline studies are waived for lentils, dry peas and flax for the present use pattern.

Processed food/feed

A canola processing study was used in lieu of a flax processing study. In this study, tepraloxydim was applied to canola at 100 g a.i./ha along with the Dash HC adjuvant (1 L/ha) and the canola seed was processed into canola meal, crude oil and refined oil fractions. A comparison of the residues in the canola seed with those in each of the processed fractions resulted in concentration factors of 0.70–0.94, 0.19–0.25 and 0.07–0.18 for meal, crude and refined oils, respectively. Therefore, MRLs for flax will cover residues of tepraloxydim in flax meal or oils. It is not necessary to consider processing factors for legume vegetables for the case of lentils and dry peas since there are no edible processed fractions from these commodities that can result in concentration of the residue.

Meat/Milk/Poultry/Eggs

Lactating cattle were administered 5, 15 and 50 ppm of a 1:1 weight ratio of tepraloxydim and 5-OH-DP in the diet for 28 days. Based on the fact that 5-OH-DP was the predominant metabolite in plant metabolism studies, the feeding approach is acceptable. The maximum theoretical dietary burden (MTDB) for cattle is 0.20 ppm. The expected residues resulting from cattle feeding at 25× the MTDB are ≤0.15 ppm for muscle, liver, kidney and fat. The expected residues resulting from cattle feeding at 250× the MTDB is 0.06 ppm for milk. For milk, 250× the MTDB was the only feeding level studied.

Laying hens were administered 5, 15 and 50 ppm of a 1:1 weight ratio of tepraloxydim and 5-OH-DP in the diet for 34 days. The MTDB for poultry is 0.05 ppm. The expected residues resulting from poultry feeding at 100× the MTDB is 0.20 ppm for eggs, 0.17 ppm for muscle, 0.73 ppm for liver and 0.19 ppm for fat.

Because of the exaggerated feeding levels, MRLs that are based on the LOQ should be established for animal commodities. Specifically, the MRLs shoudl be established at 0.03 ppm for milk and at 0.15 ppm for all other animal commodities.

Dietary risk assessment

The proposed domestic use of tepraloxydim on lentils, dry peas and flax does not pose an unacceptable chronic or acute dietary (both food and water) risk to any segment of the population, including infants, children, adults and seniors.

For this assessment, chronic and acute dietary exposure assessments were conducted to determine exposure and risk that would result from the use of tepraloxydim on lentils, flax and dry peas in Canada, as well as soybeans, cotton and canola commodities imported into Canada from the United States. The assessment assumed maximum residue limits and it was assumed that 100% of the crops are treated. For the chronic dietary risk assessment, the risk estimate for the representative population subgroups ranged from 12.5 to 55.7% of the ADI (ADI = 0.02 mg/kg bw). The dietary risk estimates were below the level of concern (100% ADI) for the general population and all of the population subgroups. The acute dietary exposure for females 13 years of age and over is 5.06% (ARfD = 0.13 mg/kg bw).

Since the current proposed uses of tepraloxydim are restricted to agricultural use patterns, the aggregated exposure assessment that was conducted included dietary exposure from food and water only. The acute and chronic aggregate exposures are acceptable and do not exceed the level of concern.

5.0 Fate and behaviour in the environment

5.1 Physical and chemical properties relevant to the environment

Tepraloxydim is very soluble in water (430–7250 mg/L) under environmentally relevant pH conditions. The low values for vapour pressure (2.7×10^{-7} hPa at 25°C) and Henry's Law constant ($<8.74 \times 10^{-6}$ Pa.m^3/mole) indicate that tepraloxydim has a low potential to volatilize from moist soil and water surfaces. Tepraloxydim has a low potential for bioconcentration/bioaccumulation in organisms ($\log K_{ow} = 1.5$). The dissociation constant value ($pK_a = 4.58$) indicates that tepraloxydim dissociates maximally under acidic conditions and, therefore, exists as an anion in environmentally relevant pH conditions. Tepraloxydim has a potential for phototransformation in the environment, as the UV–visible spectra indicates an absorption maximum at 290–300 nm.

5.2 Abiotic transformation

Hydrolysis of tepraloxydim is pH and temperature dependent (Appendix III, Table 1). Tepraloxydim hydrolyzes slowly under neutral and alkaline conditions, but hydrolyzes rapidly under acidic conditions (half-life 3.5–24.4 days). At higher temperatures, however, it hydrolyzes rapidly under neutral and alkaline conditions (half-lives of 21.4 and 16.8 days at pH 7 and pH 9, respectively). Hydrolysis is considered an important route of transformation of tepraloxydim under acidic conditions, whereas in neutral and alkaline conditions it may be a route of transformation at elevated temperatures.

Two major transformation products, DP-2 (maximum of 68% of applied radioactivity) and DP-8 (maximum of 20% of applied radioactivity), were detected under acidic conditions at 22, 35 and 45°C.

Tepraloxydim phototransformed rapidly on a loamy sandy soil with a half-life of one day, which indicates that phototransformation is an important route of transformation in the soil environment. Only five percent of the applied radioactivity was detected at the end of four days continuous irradiation. Three major transformation products, GP (22% of applied radioactivity), FP (18%) and DP-1 (11%), were detected at four days post-treatment. Two minor transformation products, DP-2 (5% of applied radioactivity) and DP-6 (4%), were also identified. The half-life values indicate that phototransformation would also be an important route of transformation for DP-2 (4 days), DP-6 (3 days) and GP (12 days) in the soil environment.

In the aquatic environment, the half-lives of 0.7 days at pH 5, 1.5 days at pH 7 and 1.6 days at pH 9 indicate that phototransformation in water would be an important route of transformation. Four major transformation products, DP-1 (50% at pH 5), DP-2 (19% at pH 7), GP (20% at pH 5), and DP-6 (13% at pH 9) were detected (Appendix III, Table 3). Half-lives of 14, 6 and 7 days for DP-1, DP-2 and DP-6, respectively, indicate that phototransformation would be an important route of transformation for these transformation products in the aquatic environment.

In a 24-hour volatilization study, 4 and 8% of the applied amount volatilized from soil and plant surfaces, respectively. These results indicate that tepraloxydim has a low potential for volatilization under field conditions, which is in agreement with its low vapour pressure and Henry's Law constant (Section 5.1).

5.3 Biotransformation

Tepraloxydim biotransformed rapidly in a sandy loam soil under aerobic conditions with first-order half-lives of 5.3 and 9 days in cyclohexene ring-labelled and tetrahydropyran ring-labelled [^{14}C] tepraloxydim studies, respectively. Half-life values indicate that tepraloxydim is non-persistent in the terrestrial environment under aerobic conditions. The DT_{90} values ranged from 17.7 to 28 days. No residues of parent compound were detected after 30-days post-treatment. No major transformation products were detected at any time during the 360-day study period. There were, however, three minor transformation products: DP-2 (maximum of 9%), DP-1 (maximum of 3%) and DP-4 (maximum of 2.4%) (Appendix III, Table 2). The maximum concentrations of non-extractable [^{14}C] residues were 22 and 25% of the applied radioactivity in cyclohexene and tetrahydropyran ring-labelled [^{14}C] tepraloxydim studies, respectively. Maximum total $^{14}CO_2$ evolved during the 360-day study period, ranging from 58 to 65% of the applied radioactivity.

Under anaerobic conditions, tepraloxydim transformed in the flooded soil system with a first-order half-life and a DT_{90} value of 3.2 months and 10.5 months, respectively. The first-order half-lives in water and soil were 3.2 and 3 months, respectively. Half-life values indicate that tepraloxydim is moderately persistent in flooded soils under anaerobic conditions. One major transformation product, DP-1 (12% of applied radioactivity), and two minor transformation products, DP-2 and DP-6, were detected. Residues in the soil phase increased over time; nonextractable [^{14}C] residues in the solid phase accounted for a maximum of 29.8% of the applied radioactivity. Total $^{14}CO_2$ accounted for 26.4% of the applied radioactivity during the 12-month study period. Organic [^{14}C] volatiles were negligible.

Tepraloxydim transformed in an aerobic sediment/water system, with half-lives of 48.6 days and 171.4 days in the flooded sandy loam and sand sediment/water systems, respectively. In the aqueous phase, the corresponding values were 41 and 129 days. The DT_{90} values for the sediment/water system and aqueous phase were 162.5 and 136.2 days, respectively. The concentration of parent compound at the end of the 100-day study period ranged from 21 to 58% of the applied amount (sum of the Z- and E-isomers). One major transformation product, DP-1, (11% of the applied radioactivity), two minor transformation products, DP-1 and DP-6, and seven unidentified minor transformation products were detected. The ^{14}C residues in the sediment and particulate matter increased over time due to partitioning and incorporation from the water phase.

5.4 Mobility

Tepraloxydim is highly to very highly mobile in sand, sandy loam, loamy sand, loam and clay soils (K_d = 0.011 to 1.5 and K_{oc} = 3.7 to 77.2) (Appendix III, Table 1). During the adsorption phase, 7 to 67% of the applied amount was adsorbed to soil particles. At the end of the desorption phase, 38–100% of the adsorbed amount was desorbed. Desorption K_d values were higher in loamy sand and loam soils and lower in clay soil than those obtained for adsorption.

The transformation product tepraloxydim-imine (DP-1) is moderately to very highly mobile in soils (K_d = 0.47 to 3.9 and K_{oc} = 48 to 1107). During the adsorption phase, the percent of applied adsorbed ranged from 15.1 to 63.5. At the end of the desorption phase, 28–68% of the adsorbed amount was desorbed. The desorption K_d and K_{oc} values ranged from 0.17 to 2.5 and 24 to 705, respectively.

Another major transformation product, tepraloxydim-oxozole (DP-2), is moderately to highly mobile in loamy, sandy loam and loamy sand soils, and of low mobility in silt loam soils (K_d = 0.35 to 14.7). During the adsorption phase, the percent of applied adsorbed ranged from 11 to 88%. At the end of desorption phase, 15–68% of the adsorbed amount was desorbed. Desorption K_d and K_{oc} values ranged from 0.11 to 12.5 and 22 to 3561, respectively.

5.5 Dissipation and accumulation under field conditions

Under field conditions, tepraloxydim dissipated rapidly with DT_{50} values of 6, 3, 12 and 9 days at the Manitoba, Saskatchewan, Alberta and North Dakota sites, respectively (Appendix III, Table 1). These values indicate that tepraloxydim is non-persistent under field conditions. The calculated DT_{90} values for Manitoba, Saskatchwan, Albarta and North Dakota sites were 36, 20, 76 and 31 days, respectively; however, no residues of the parent compound were detected after 30 days. Tepraloxydim has, therefore, no potential for carryover into the following season.

Two major transformation products were detected in the 0–5 cm soil depth (Appendix III, Table 2): DP-1, with a maximum concentration of 12% of applied at the North Dakota site, and DP-2, with maximum concentrations of 17 and 15% of applied at the Alberta and North Dakota sites, respectively. The DT_{50} value of 28 days indicate that DP-1 is slightly persistent in soils. The DT_{50} values of 235, 198, 212 and 210 days for the Manitoba, Saskatchwan, Alberta and North Dakota sites, respectively, indicate that DP-2 is persistent in soils and indicate that it would be carried over to the following season. No residues of DP-1 and only 2 % of DP-2 were detected at the end of the 540-day study period.

No residues were detected below a depth of 5 cm at any site at any time; consequently, the parent compound and transformation products have a low potential to leach and contaminate groundwater under field conditions. As leaching was minimal and no volatilization is expected, transformation would appear to be the major route of dissipation under field conditions.

5.6 Bioaccumulation

Bioconcentration factors (BCFs, 0.76–2.3), uptake rate constant (1.0) and depuration half-life values (0.92) in fish indicate that tepraloxydim would not be expected to bioaccumulate in organisms.

5.7 Summary of fate and behaviour in the terrestrial environment

Tepraloxydim transforms rapidly in soils and is non-persistent (lab $t_{1/2}$ = 5.3 to 9 days and field DT_{50} = 3 to 12 days). Tepraloxydim is, however, moderately persistent in soils under anaerobic conditions (lab $t_{1/2}$ = 3 months). Important routes of transformation are phototransformation ($t_{1/2}$ = 1.1 days), biotransformation (aerobic $t_{1/2}$ = 5.3 to 9 days) and hydrolysis in acidic conditions ($t_{½}$ at pH 5 = 5.1 and 24.4 days at 35 and 22°C, respectively).

Five major transformation products were detected in soils under laboratory conditions: DP-2 and DP-8 in the hydrolysis studies; DP-1, GP and FP in the phototransformation studies; and DP-1 in the anaerobic biotransformation studies. The minor transformation products detected were DP-6, DP-10 and DP-4. Under field conditions, however, only two major transformation products, DP-1 and DP-2, and no minor transformation products were detected. DP-1 was slightly persistent (DT_{50} = 28 days) and DP-2 was persistent in soils (field DT_{50} = 198-235 days). Residues of these products were, however, negligible at the end of the 540-day study period.

Although laboratory adsorption studies indicated that tepraloxydim is highly mobile (K_d = 0.042 to 1.5 and K_{oc} = 3.7 to 77.2), it did not leach beyond a soil depth of 5 cm under field conditions at any of the four test sites, probably due to rapid transformation. Tepraloxydim has, therefore, a low potential to contaminate groundwater. As leaching was minimal and no volatilization was expected, transformation appears to be the route of dissipation under field conditions. The DT_{90} values (20 to 76 days) and low concentrations detected 30-days postapplication indicate that tepraloxydim has a negligible potential for carryover to the next crop season.

5.8 Summary of fate and behaviour in the aquatic environment

Tepraloxydim transforms rapidly in the aquatic environment by phototransformation ($t_{1/2}$ = 0.7 to 1.6 days) and by acid hydrolysis ($t_{1/2}$ at pH 5 = 5.1 and 24.4 days at 35 and 22°C, respectively). Phototransformation is an important route of transformation for tepraloxydim in the aquatic environment. Tepraloxydim is moderately persistent in aquatic systems under aerobic conditions ($t_{1/2}$ = 48.6–170.4 days). A soil/water anaerobic study indicated that tepraloxydim is also moderately persistent under anaerobic conditions in aquatic systems.

Five major transformation products were detected in aquatic systems: DP-2 and DP-8 in hydrolysis studies; DP-1, DP-2, DP-6 and GP in phototransformation studies; and DP-1 in aerobic/anaerobic biotransformation studies. The BCFs(0.76–2.3), uptake rate constant (1.0) and depuration half-life values (0.92) in fish indicate that tepraloxydim has a low potential for bioaccumulation in organisms, which is in agreement with its low log K_{ow} of 1.5.

5.9 Summary of fate and behaviour in air

Tepraloxydim has a very low vapour pressure (2.7×10^{-7} hPa at 25°C) and a low Henry's Law constant ($<8.74 \times 10^{-6}$ Pa.m^3/mole and 1/H = 2.8E+10), and only 4 and 8% of the applied amount volatilized from soil and plant surfaces, respectively, during a 24-hour study period. These values indicate that tepraloxydim is essentially non-volatile and no significant volatilization is expected. Atmospheric contamination is, therefore, not considered to be an important route of exposure with the proposed use.

5.10 Expected environmental concentrations (EECs)

The EECs in soil, water and food sources were estimated assuming a scenario in which the maximum Canadian label rate of 250 mL (258 g) EP or 50 g a.i./ha is applied once to a bare soil, oversprayed on aquatic systems and plants, respectively. The EECs in various environmental media are summarized in Table 5.10.1.

Table 5.10.1 Maximum EEC in soil, water and diets of birds and mammals

Organism	EEC (TGAI)	EEC (EP)	EEC (EP+Dash HC)
Soil (mg/kg soil)	0.022	0.115	0.369
Water (mg/L water)	0.033	0.172	0.552
Bobwhite quail diet (mg/kg dw diet)	8.75		
Mallard duck diet (mg/kg dw diet)	1.69		
Rat diet (mg/kg dw diet)	25.22		
Mouse (mg/kg dw diet)	25.07		
Rabbit (mg/kg dw diet)	37.72		

Drinking Water: The estimated environmental concentrations in drinking water as a result of leaching or runoff are summarized in Table 5.10.2.

Table 5.10.2 Level I EECs in drinking water

Groundwater (µg a.i./L)		Surface Water (µg a.i./L)			
		Reservoir		Dugout	
Acute[1]	Chronic[2]	Acute[3]	Chronic[4]	Acute[3]	Chronic[4]
2.4	2.1	1.5	0.4	1.6	1

1 90th percentile of daily average concentrations
2 90th percentile of yearly average concentrations
3 90th percentile of yearly peaks
4 90th percentile of yearly averages

6.0 Effects on non-target species

6.1 Effects on terrestrial organisms

Tepraloxydim has no adverse effects on earthworms up to 400 mg a.i./kg soil (Appendix III, Table 6). With the EPs, however, the no observed effect concentration (NOEC) and LC_{50} were 781 and >1390 mg EP/kg soil, respectively. The corresponding values for the combination product of EP plus Dash HC were 63 mg EP plus 225 mg Dash HC and 120 mg EP plus 437 mg Dash HC mg/kg soil. These values indicate that tepraloxydim would adversely affect the earthworms at concentrations greater than 63 mg EP/kg soil when used with Dash HC adjuvant. The LC_{50}s for tepraloxydim (>25 µg a.i./bee) and the combination product of EP plus Dash HC (40 µg EP + 160 µg Dash HC/bee) indicate that they are non-toxic to bees on an acute basis.

Tepraloxydim is non-toxic to wild birds on an acute basis (LD_{50} >2000 mg a.i./kg bw) and on a short-term dietary basis (LC_{50} >5869 mg a.i./kg diet), and no adverse effects on reproductive performance were observed up to 1000 mg a.i./kg diet. Tepraloxydim is also non-toxic to wild mammals on an acute basis (LD_{50} >2000 mg a.i./kg bw) and no adverse effects on reproductive performance were observed up to 500 mg a.i./kg diet. Tepraloxydim is, however, phytotoxic to terrestrial vascular plants. The NOEC and EC_{25} values for seedling emergence were 28.2 and 91.3 g EP/ha (plus 858.28 g Dash HC/ha), respectively. The corresponding values for the vegetative vigour were 9.4 and 25.2 g EP/ha (plus 858.28 g Dash HC/ha).

6.2 Effects on aquatic organisms

Equinox EC is moderately toxic to freshwater invertebrates (*Daphnia* LC_{50} = 7.44 EP mg/L) on an acute basis (Appendix III, Table 7). Tepraloxydim is slightly toxic to warm water fish (LC_{50} >78 mg a.i./L) and non-toxic to cold water fish (LC_{50} >100 mg a.i./L); however, it is moderately toxic to fish when used as an end-use product (LC_{50} = 4.45 mg/L) and as a combination product of EP plus Dash HC (LC_{50} = 0.91 EP + 1.92 Dash HC mg/L). The transformation product DP-1 is non-toxic to fish (LC_{50} >96.2 mg/L). Tepraloxydim is non-toxic to marine invertebrates and fish (LC_{50} >120 mg a.i./L), but moderately to highly toxic to these organisms when used as an end-use product (LC_{50} = 0.5–1.35 mg EP/L). Studies on bioaccumulation in fish (BCF 0.76–2.3, uptake rate constant 1.0 and depuration half-life values 0.92) and the log K_{ow} of 1.5 indicate that tepraloxydim has a low potential for bioaccumulation in organisms. Tepraloxydim will inhibit the algal growth at concentrations greater than 10.2 mg a.i./L water; however, the NOEC of the end-use product was 0.4 mg EP/L. Tepraloxydim is phytotoxic to aquatic plants and would adversely affect them at concentrations greater than 1.11 mg a.i./L (NOEC and EC_{50} for *Lemna* sp = 1.11 and 6.47 mg a.i./L, respectively).

6.3 Effects on biological methods of sewage treatment

Not required by the PMRA.

6.4 Risk characterization

6.4.1 Environmental behaviour

Tepraloxydim rapidly transforms in soils by acid hydrolysis, photolysis and biotransformation. It is non-persistent in soils and has a low potential for residue carryover. Five major transformation products (DP-1, DP-2, DP-8, GP and FP) were identified in laboratory studies; however, only DP-1 and DP-2 were detected under field conditions. DP-1 is slightly persistent, whereas DP-2 is persistent in soils under field conditions. Although laboratory studies indicated that tepraloxydim and its transformation products are highly mobile in soils, they did not leach under field conditions, probably due to rapid transformation and therefore have a low potential to contaminate groundwater. Tepraloxydim has a negligible potential for residue carryover to the following crop season.

In the aquatic environment, tepraloxydim transforms rapidly by phototransformation and by acid hydrolysis. Tepraloxydim is moderately persistent in aquatic systems. Tepraloxydim has a low potential for bioaccumulation in organisms. Five major transformation products (DP-1, DP-2, DP-6, DP-8 and GP) were detected in aquatic systems in laboratory studies. Phototransformation is an important route of transformation for tepraloxydim and its transformation products in the aquatic environment.

6.4.2 Terrestrial organisms

Risk to terrestrial organisms was assessed using the NOEL or NOEC values of the most sensitive species. The proposed use of Equinox EC suggests that exposure is likely to occur through the consumption of treated foliage and food sources, with the greatest risk arising from oral ingestion of treated foliage or diet. Dietary intake (DI) was estimated from the information on the food consumption (FC) and the EEC of tepraloxydim in the diet (DI = FC × EEC). Assessment of acute risk to wild birds and mammals was based on the number of days of intake of treated foliage that would result in observable effects. Dietary and reproductive risk to birds and mammals and acute risk to bees and soil organisms were assessed using RQ (Risk Quotient, EEC/NOEC) values.

Assessment of risk to terrestrial organisms (Appendix III, Table 8) indicated that the proposed use of Equinox EC with Dash HC will not pose a risk to terrestrial invertebrates such as earthworms and bees. The proposed use of Equinox EC will also not pose a risk to wild birds and mammals on an acute and dietary basis and also will not affect their reproductive performance. The proposed maximum application rate of Equinox EC with Dash HC adjuvant will not pose a risk to non-target terrestrial vascular plants.

6.4.3 Aquatic organisms

Risk to aquatic organisms was assessed using the EEC values in Table 5.10.1 and the NOEC of most sensitive species (Appendix III, Table 9). The RQ values (<0.1) indicate that the proposed use of Equinox EC with Dash HC will not pose a risk to freshwater organisms such as fish, invertebrates, algae and aquatic plants. Risk to marine organisms was not assessed, as there is no exposure to marine organisms with the proposed use.

6.5 Label statements

The following label statement is required under DIRECTIONS FOR USE on the label of Equinox EC:

"Do not apply during periods of dead calm or when winds are gusty. Do not overspray non-target terrestrial or aquatic habitats. Do not contaminate aquatic habitats when cleaning and rinsing spray equipment or containers.

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture."

Equinox EC and Dash HC contain petroleum distillates (USEPA List 2), which are toxic to aquatic organisms. The following precautionary label statement is required:

"This product contains a petroleum distillate which is moderately to highly toxic to aquatic organisms. Avoid contamination of aquatic systems during application. Do not contaminate these systems through direct application, disposal of wastes or cleaning equipment."

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended use

Tepraloxydim is formulated in one end-use herbicide product. Equinox EC is an emulsifiable concentrate formulation that has a guarantee of tepraloxydim of 200 g/L and must be applied with the adjuvant Dash HC.

Equinox EC is a selective herbicide proposed for use as a postemergence application to flax (including low linolenic acid and sulfonyl urea tolerant varieties), lentils and dry peas grown in the Prairie Provinces and the Peace River region of British Columbia for the control of specific grass weeds. Equinox EC must be applied with Dash HC adjuvant at 0.41–0.62% v/v (i.e., 0.41 L Dash HC/100 L spray solution) in a spray volume of 100 L/ha with a maximum of one application per year using ground equipment only.

There are two proposed and accepted rates of application for Equinox EC. Equinox EC applied at a rate of 0.165 L/ha (33 g a.i./ha) plus Dash HC adjuvant at 0.41% v/v is effective for the control of wild oats (*Avena fatua*), green foxtail (*Setaria viridis*), volunteer barley (*Hordeum vulgare*) and volunteer wheat (*Triticum aestivum*) at the 1–6 leaf stage up to two tillers. Equinox EC applied at a rate of 0.250 L/ha (50 g a.i./ha) plus Dash HC adjuvant at 0.62% v/v is effective for the control of quackgrass (*Agropyron* when weed densities are high and overlapping, when staging is late or when weeds are under stress and not growing as actively due to moisture or temperature stress.

There are no rotational cropping restrictions necessary for Equinox EC.

Proposed tank mixes with Equinox EC plus Dash HC adjuvant include Buctril M (MCPA + bromoxynil) at 1.0 L/ha or Flaxmax (MCPA + clopyralid) at 2.0 L/ha when applied to flax.

7.1.2 Mode of action

Tepraloxydim belongs to the general class of herbicides termed cyclohexanediones. The primary mode of action is through inhibition of ACCase, which impacts fatty acid biosynthesis and lipid metabolism. In addition, the cell membrane functions are blocked and cell division is affected. Sensitive grass species exhibit symptoms within a few days in the form of cessation of growth and development. The young leaves turn yellow within 7–21 days and some grass species develop a reddish colouration. Necrotic spots then form on the leaves, leading to subsequent death.

7.1.3 Crops

Value data were provided in support of use on flax, dry peas and lentils.

7.1.4 Effectiveness against pests

7.1.4.1 Equinox EC + Dash HC adjuvant

The efficacy data package provided in support of the requested weeds reported the results of trials conducted in five crops. These crops were canola, mustard, flax, dry peas and lentils. The efficacy data generated in each of these crops has been used in the assessment of the efficacy of tepraloxydim as these data support the overall claim of control of the proposed weeds.

7.1.4.1.1 Wild oats (*Avena fatua*)

The efficacy data package provided in support of the claim of control of wild oats consisted of 92 trials conducted over four years across the Prairie Provinces in five crops (canola, mustard, flax, dry peas and lentils). Control averaged 92% at mid-season (<40 DAT) and 94% at late season (>40 DAT) (Table 7.1.4.1.1.1).

The efficacy data package indicated the control of wild oats is similar in all of the crops tested (Table 7.1.4.1.1.2).

The 33 g tepraloxydim/ha + 0.41% v/v Dash HC rate provides acceptable control of wild oats.

Table 7.1.4.1.1.1 Wild oats control in all crops

Treatment	Rating Period	# data points reporting % control				Mean % control	n
		90–100%	80–89%	60–79%	<60%		
33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	64	15	2	2	92	83
	late season	73	11	2		94	86

Table 7.1.4.1.1.2 Wild oats control in various crops with the application of 33 g tepraloxydim/ha + 0.41% v/v Dash HC

Crop	# trials / # years / # locations	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Canola	35 / 3 / 20	mid-season	25	5		2	91	32
		late season	28	5			94	33
Mustard	7 / 2 / 5	mid-season	5	1			94	6
		late season	7				98	7
Flax	23 / 3 / 15	mid-season	15	4	2		91	21
		late season	18	1	1		95	20
Dry peas	15 / 3 / 10	mid-season	11	2			93	13
		late season	10	3	1		93	14
Lentils	12 / 3 / 8	mid-season	8	3			93	11
		late season	10	2			94	12

7.1.4.1.2 Green foxtail (*Setaria viridis*)

The efficacy data package provided in support of the claim of control of green foxtail consisted of 61 trials conducted over four years across the Prairie Provinces in five crops (canola, mustard, flax, dry peas and lentils). Control averaged 93% at mid-season (<40 DAT) and 94% at late season (>40 DAT) (Table 7.1.4.1.2.1).

The efficacy data package indicated the control of green foxtail is similar in all of the crops tested (Table 7.1.4.1.2.2).

The 33 g tepraloxydim/ha + 0.41% v/v Dash HC rate provides acceptable control of green foxtail.

Table 7.1.4.1.2.1 Green foxtail control in all crops

Treatment	Rating period	# data points reporting % control				Mean % control	n
		90–100%	80–89%	60–79%	<60%		
33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	44	14			93	58
	late season	43	9			94	52

Table 7.1.4.1.2.2 Green foxtail control in various crops with the application of 33 g tepraloxydim/ha + 0.41% v/v Dash HC

Crop	# trials / # years / # locations	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Canola	19 / 3 / 10	mid-season	15	4			94	19
		late season	16	2			95	18
Mustard	6 / 2 / 4	mid-season	4	2			94	6
		late season	4	1			94	5
Flax	19 / 3 / 12	mid-season	13	4			93	17
		late season	13	4			94	17
Dry peas	10 / 3 / 8	mid-season	8	2			93	10
		late season	7	1			94	8
Lentils	7 / 4 / 4	mid-season	4	2			93	6
		late season	3	1			94	4

7.1.4.1.3 Volunteer barley (*Hordeum vulgare*)

The efficacy data package provided in support of the claim of control of volunteer barley consisted of 85 trials conducted over four years across the Prairie Provinces in five crops (canola, mustard, flax, dry peas and lentils). Control averaged 90% at mid-season (<40 DAT) and 93% at late season (>40 DAT) (Table 7.1.4.1.3.1).

The efficacy data package indicated the control of volunteer barley is similar in all of the crops tested (Table 7.1.4.1.3.2).

The 33 g tepraloxydim/ha + 0.41% v/v Dash HC rate provides acceptable control of volunteer barley.

Table 7.1.4.1.3.1 Volunteer barley control in all crops

Treatment	Rating period	# data points reporting % control				Mean % control	n
		90–100%	80–89%	60–79%	<60%		
33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	53	16	14	1	90	84
	late season	55	17	5		93	77

Table 7.1.4.1.3.2 Volunteer barley control in various crops with the application of 33 g tepraloxydim/ha + 0.41% v/v Dash HC

Crop	# trials / # years / # locations	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Canola	29 / 3 / 16	mid-season	20	4	4	1	90	29
		late season	21	6	1		92	28
Mustard	8 / 2 / 5	mid-season	6	1	1		93	8
		late season	7	1			96	8
Flax	21 / 3 / 15	mid-season	12	4	5		88	21
		late season	13	2	1		93	16
Dry peas	14 / 3 / 9	mid-season	9	3	1		92	13
		late season	6	5	1		92	12
Lentils	13 / 4 / 8	mid-season	6	4	3		89	13
		late season	8	3	2		91	13

7.1.4.1.4 Volunteer wheat (*Triticum aestivum*)

The efficacy data package provided in support of the claim of control of volunteer wheat consisted of 81 trials conducted over four years across the Prairie Provinces in five crops (canola, mustard, flax, dry peas and lentils). Control averaged 92% at mid-season (<40 DAT) and 93% at late season (>40 DAT) (Table 7.1.4.1.4.1).

The efficacy data package indicated the control of volunteer wheat is similar in all of the crops tested (Table 7.1.4.1.4.2).

The 33 g tepraloxydim/ha + 0.41% v/v Dash HC rate provides acceptable control of volunteer wheat.

Table 7.1.4.1.4.1 Volunteer wheat control in all crops

Treatment	Rating period	# data points reporting % control				Mean % control	n
		90–100%	80–89%	60–79%	<60%		
33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	64	9	5	1	92	79
	late season	56	13	4		93	73

Table 7.1.4.1.4.2 Volunteer wheat control in various crops with the application of 33 g tepraloxydim/ha + 0.41% v/v Dash HC

Crop	# trials / # years / # locations	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Canola	26 / 3 / 15	mid-season	20	4	1	1	91	26
		late season	18	7			93	25
Mustard	8 / 2 / 5	mid-season	7	1			95	8
		late season	7				98	7
Flax	21 / 3 / 13	mid-season	18	1	2		92	21
		late season	13	3	1		94	17
Dry peas	15 / 3 / 10	mid-season	11	2			94	13
		late season	10	3			94	13
Lentils	11 / 4 / 8	mid-season	8	1	2		92	11
		late season	8		3		89	11

7.1.4.1.5 Quackgrass (*Agropyron repens*)

The efficacy data package provided in support of the claim of control of quackgrass consisted of 26 trials conducted over three years across the Prairie Provinces in three crops (canola, flax and dry peas). Control averaged 87% at mid-season (<40 DAT) and 81% at late season (>40 DAT) (Table 7.1.4.1.5.1). The efficacy data package indicated the control of quackgrass is similar in all of the crops tested (Table 7.1.4.1.5.2).

The draft label indicates that regrowth of quackgrass will not be significant until 6–8 weeks after treatment. Therefore, based on this qualification and the assessment of the efficacy data provided in support of the claim of control of quackgrass, this weed is acceptable to appear on the Equinox EC label at the requested rate of 50 g a.i./ha + 0.62% v/v Dash HC.

Table 7.1.4.1.5.1 Quackgrass control in all crops with 33 g a.i. tepraloxydim/ha + 0.41% v/v Dash and 50 g a.i. tepraloxydim/ha + 0.62% v/v Dash

Treatment	Rating period	# data points reporting % control				Mean % control	n
		90–100%	80–89%	60–79%	<60%		
33 g a.i. tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	2	1	2	1	76	6
	late season	1		1	2	64	4
50 g tepraloxydim/ha + 0.62% v/v Dash HC	mid-season	9	9	1	1	87	20
	late season	5	9	5	2	81	21

Table 7.1.4.1.5.2 Quackgrass control in various crops with the application of 33 g a.i. tepraloxydim/ha + 0.41% v/v Dash HC and 50 g a.i. tepraloxydim/ha + 0.62% v/v Dash HC

Crop	# trials # years # location	Rate application	Rating period	# data points reporting % control				Mean % control	n
				90–100%	80–89%	60–79%	<60%		
Canola	12 / 2 / 11	33 g a.i. tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	1			1	70	2
			late season					—	—
		50 g a.i. tepraloxydim/ha + 0.62% v/v Dash HC	mid-season	4	5			88	9
			late season	3	4	3		85	10
Flax	11 / 2 / 10	33 g a.i. tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	1		1		75	2
			late season				2	45	2
		50 g a.i. tepraloxydim/ha + 0.62% v/v Dash HC	mid-season	5	2	1	1	85	9
			late season	2	4	1	2	79	9
Dry Peas	3 / 3 / 2	33 g a.i. tepraloxydim/ha + 0.41% v/v Dash HC	mid-season		1	1		82	2
			late season	1		1		84	2
		50 g a.i. tepraloxydim/ha + 0.62% v/v Dash HC	mid-season		2			85	2
			late season		1	1		75	2

7.1.4.2 Establishing lowest effective rate

The efficacy data package indicated the application of 33 g a.i./ha + 0.41% v/v Dash HC will provide acceptable control of the annual grasses appearing on the Equinox EC label. The efficacy data package also indicated rates lower than 33 g a.i./ha may provide acceptable control of the annual grasses appearing on the Equinox EC label.

The rates examined were 20 and 25 g a.i./ha using Dash HC at 0.41–0.50% v/v.

For the 20 g a.i./ha rate, the data package consisted of seven trials conducted over two years over seven locations in the Prairie Provinces (Table 7.1.4.2.1).

Table 7.1.4.2.1 Annual grass control with Equinox EC at 20 g a.i./ha + Dash HC at 0.41–0.50% v/v

Weed	Rating period	# data points reporting % control				n	Mean % Control
		90–100%	80–89%	60–79%	<60%		
Green foxtail	14–40 DAT	2	1	2		5	86
	+41 DAT	2		3		5	83
Volunteer barley	14–40 DAT	4	2	1		7	86
	+41 DAT	3	1	3		7	83
Volunteer wheat	14–40 DAT	1	2	1		4	79
	+41 DAT	1		4		5	70
Wild oats	14–40 DAT	2	2	2		6	83
	+41 DAT	2		4		6	81

The data indicated Equinox EC at 20 g a.i./ha + Dash HC at 0.41–0.50% v/v provided inconsistent control of green foxtail, volunteer barley and wild oats, with about one half of the trials providing less than 80% control. The data indicated that volunteer wheat is not controlled by the 20 g a.i./ha rate of Equinox EC.

Based on the data provided, the application of Equinox EC at 20 g a.i./ha + Dash HC at 0.41–0.50% v/v does not provide a consistent and acceptable level of control for the annual grasses requested to appear on the Equinox EC label.

For the 25 g a.i./ha rate, the data package consisted of four trials conducted in one year over four locations in the Prairie Provinces (Table 7.1.4.2.2). The data provided testing Equinox EC at 25 g a.i./ha + Dash HC at 0.41% v/v indicated this rate may provide a consistent and acceptable level of control of the annual grasses requested to appear on the Equinox EC label. However, four trials are insufficient data upon which to base a regulatory decision.

Table 7.1.4.2.2 **Annual grass control with Equinox EC at 25 g a.i./ha + Dash HC at 0.41% v/v**

Weed	Rating period	# data points reporting % control				n	Mean % Control
		90–100%	80–89%	60–79%	<60%		
Green foxtail	14–40 DAT	2				2	91
	+41 DAT	1				1	100
Volunteer barley	14–40 DAT	2	2			4	90
	+41 DAT	2	2			4	89
Volunteer wheat	14–40 DAT	2	2			4	89
	+41 DAT	2	1	1		4	89
Wild oats	14–40 DAT	3	1			4	93
	+41 DAT	4				4	96

The data package also contained trials testing the efficacy of Equinox EC at the rate of 25 g a.i./ha but used adjuvants other than Dash HC. These trials used the adjuvants Merge and Amigo. The results of the trials testing the efficacy of Equinox EC at 25 g a.i./ha with all adjuvants have been pooled and presented in Table 7.1.4.2.3. The results of these trials further support the observation that the application of Equinox EC at the rate of 25 g a.i./ha may provide a consistent and acceptable level of control of the requested annual grasses on the Equinox EC label. However, these data cannot be used to support the registration of the 25 g a.i./ha rate of Equinox EC since the adjuvants used were not the Dash HC adjuvant as requested on the Equinox EC label.

Table 7.1.4.2.3 **Annual grass control with Equinox EC at 25 g a.i./ha + an adjuvant**
These trials used the adjuvant Merge at 1.0% v/v, Amigo at 0.5% v/v or Dash HC at 0.41% v/v

Weed	Rating period	# data points reporting % control				n	Mean % Control
		90–100%	80–89%	60–79%	<60%		
Green foxtail	14–40 DAT	7	5	1		13	88
	+41 DAT	9	1	1		11	94
Volunteer barley	14–40 DAT	5	11	1	1	18	86
	+41 DAT	11	2	2	1	16	89
Volunteer wheat	14–40 DAT	7	9	2		18	87
	+41 DAT	11	2	2	1	16	90
Wild oats	14–40 DAT	15	10	3		28	89
	+41 DAT	20	1	1		22	94

Based on the results of the limited data testing the efficacy of Equinox EC at 25 g a.i./ha + Dash HC at 0.41% and the data testing the efficacy of Equinox EC at 25 g a.i./ha with other adjuvants, additional data will be required in order to fully assess the efficacy of the Equinox EC applied at rates lower than the 33 g a.i./ha rate. The rates of 25 and 30 g a.i./ha should be assessed in order to determine the lowest effective rate for the annual weeds listed on the Equinox EC label.

7.1.4.3 Tank mixes

7.1.4.3.1 Equinox EC + Dash HC + Buctril M (MCPA + bromoxynil) in flax

The efficacy data package provided in support of the subject tank mix consists of 14 trials conducted over three years, which tested the efficacy of Equinox EC at 33 g a.i./ha + Dash HC at 0.41% v/v + Buctril M at 560 g a.i./ha vs. Equinox EC at 33 g a.i./ha + Dash HC at 0.41% v/v as side-by-side treatments.

The efficacy data indicated that this tank mix provides similar control of all requested annual grass weeds on the Equinox EC label compared to Equinox EC applied alone (Table 7.1.4.3.1.1). The efficacy data indicated that this tank mix provides similar control of broadleaf weeds currently claimed on the Buctril M label compared to Buctril M applied alone (Table 7.1.4.3.1.2).

Based on the assessment of the annual grass and broadleaf weed efficacy data provided in support of the tank mixture of Equinox EC + Dash HC + Buctril M, this tank mix is acceptable to appear on the Equinox EC label at the requested rates.

Table 7.1.4.3.1.1 Annual grass control in flax with the application of 33 g tepraloxydim/ha + 0.41% v/v Dash HC and 33 g tepraloxydim/ha + 0.41% v/v Dash HC + 560 g a.i./ha Buctril M

Weed	Rate application	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Green foxtail	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	7	4			91	11
		late season	8	1	1		93	10
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	8	3			93	11
		late season	8	1			96	9
Volunteer barley	33 g tepraloxydim/ha + 0.41% v/v Dash HC+ 560 g a.i./ha Buctril M	mid-season	6	4			92	10
		late season	7	2			94	9
	33 g tepraloxydim/ha + 0.41% v/v Dash	mid-season	5	3	2		90	10
		late season	7				97	7

Weed	Rate application	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Volunteer wheat	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	6	4			92	10
		late season	8	1			94	9
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	9	1			93	10
		late season	8	1			96	9
Wild oats	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	9	3	1		91	13
		late season	11		1		93	12
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	9	4			92	13
		late season	10	1			96	11

Table 7.1.4.3.1.2 Broadleaf weed control in flax with the application of 50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M and 560 g a.i./ha Buctril M

Weed	Treatment g a.i./ha	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Wild buckwheat	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	2		4	1	77	7
		late season	1	1	4	1	69	7
	560 g a.i./ha Buctril M	mid-season	5	1	4		83	10
		late season	3	3	3	1	74	10
Redroot pigweed	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season		1	4	2	65	7
		late season	1		2	3	54	6
	560 g a.i./ha Buctril M	mid-season		2	5	1	69	8
		late season	1	2		4	55	7
Wild mustard	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	4	1			94	5
		late season	2	1	1		90	4
	560 g a.i./ha Buctril M	mid-season	5	1			94	6
		late season	4		1		91	5
Volunteer canola	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	1	2			88	3
		late season	1	1	1		82	3
	560 g a.i./ha Buctril M	mid-season	2	2			89	4
		late season	1	2	1		84	4

Weed	Treatment g a.i./ha	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Lambsquarters	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	mid-season	3	1			94	4
		late season	4				98	4
	560 g a.i./ha Buctril M	mid-season	4				95	4
		late season	4				97	4

7.1.4.3.2 Equinox EC + Dash HC+ Flaxmax (MCPA + clopyralid) in flax

The efficacy data package provided in support of the subject tank mix consisted of eight trials conducted in one year, which tested the efficacy of Equinox EC at 33 g a.i./ha + Dash HC at 0.41% v/v + Flaxmax at 660 g a.i./ha vs. Equinox EC at 33 g a.i./ha + Dash HC at 0.41% v/v as side by side treatments.

The efficacy data indicated that this tank mix provides similar control of all requested annual grass weeds on the Equinox EC label compared to Equinox EC applied alone (Table 7.1.4.3.2.1). The efficacy data indicated that this tank mix provides similar control of broadleaf weeds currently claimed on the Flaxmax label compared to Flaxmax applied alone (Table 7.1.4.3.2.2).

Based on the assessment of the annual grass and broadleaf weed efficacy data provided in support of the tank mixture of Equinox EC + Dash HC + Flaxmax, this tank mix is acceptable to appear on the Equinox EC label at the requested rate.

Table 7.1.4.3.2.1 Annual grass control in flax with the application of 33 g tepraloxydim/ha + 0.41% v/v Dash HC and 33 g tepraloxydim/ha + 0.41% v/v Dash HC + 660 g a.i./ha Flaxmax

Weed	Rate application	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Green foxtail	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	2	3			87	5
		late season	1	3	1		87	5
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	3	2			92	5
		late season	2	3			90	5
Volunteer barley	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	2	2	1		85	5
		late season	2	2	1		87	5
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	2		3		81	5
		late season	3	1	1		89	5

Weed	Rate application	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Volunteer wheat	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	3	3	2		86	8
		late season	3	4	1		88	8
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	5	1	2		87	8
		late season	3	3	1		91	7
Wild oats	33 g tepraloxydim/ha + 0.41% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	4	2	1		89	7
		late season	5	1	1		92	7
	33 g tepraloxydim/ha + 0.41% v/v Dash HC	mid-season	4	1	2		87	7
		late season	6		1		94	7

Table 7.1.4.3.2.2 Broadleaf weed control in flax with the application of 50 g tepraloxydim/ha + 0.62% v/v Dash HC + 660 g a.i./ha and Flaxmax 660 g a.i./ha Flaxmax

Weed	Treatment g a.i./ha	Rating period	# data points reporting % control				Mean % control	n
			90–100%	80–89%	60–79%	<60%		
Wild buckwheat	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	2	2	3		84	7
		late season	4	1	2		88	7
	660 g a.i./ha Flaxmax	mid-season	3	2	2		85	7
		late season	4		3		86	7
Wild mustard	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	3	2			93	5
		late season	4				95	4
	660 g a.i./ha Flaxmax	mid-season	4	1			93	5
		late season	3	2			95	5
Redroot pigweed	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season		1	6		73	7
		late season		1	3	2	69	6
	660 g a.i./ha Flaxmax	mid-season		2	5		74	7
		late season		2	2	3	66	7
Lambsquarters	50 g tepraloxydim/ha + 0.62% v/v Dash HC + 660 g a.i./ha Flaxmax	mid-season	3	1			95	4
		late season	4				98	4
	660 g a.i./ha Flaxmax	mid-season	4				95	4
		late season	4				98	4

7.1.5 Total spray volume

Based on the value data package provided, Equinox EC + Dash HC must be applied in a spray volume of 100 L/ha.

7.2 Phytotoxicity to target plants (including different cultivars) or to target plant products

7.2.1 Equinox EC + Dash HC in flax

Equinox EC is proposed for use as a postemergent herbicide applied when flax is from emergence to 35 cm at a maximum rate (1×) of 0.25 L/ha (50 g a.i./ha) + Dash HC at 0.62% v/v.

Fifty-two (52) trials conducted across the Prairie Provinces over eight years using ten varieties reported crop tolerance of flax following application of Equinox EC. The varieties tested included low linolenic acid and sulfonyl urea tolerant flax.

The crop tolerance data indicated that flax provides acceptable crop tolerance to the application of Equinox EC + Dash HC at the maximum requested rate and the 2× rate (Table 7.2.1.1). The crop yield data indicated that the application of Equinox EC + Dash HC at the maximum requested rate and the 2× rate provides increased yields compared to the untreated check (Table 7.2.1.2).

Based on an assessment of the crop tolerance and yield data provided in support of flax, this crop is acceptable to appear on the Equinox EC label at the maximum requested rate of 50 g a.i./ha + Dash HC at 0.62% v/v.

Table 7.2.1.1 Crop tolerance of flax to applications of tepraloxydim + Dash HC

Treatment	DAT	0% Crop damage	<5% Crop damage	5–10% Crop damage	>10% Crop damage	n	Mean
50 g tepraloxydim/ha + 0.62% v/v Dash HC	1–14	14	4	3		21	1.6
	15–31	19	2	0		21	0.3
	32–80	17	1	2		20	0.6
100 g tepraloxydim/ha + 1.24% v/v Dash HC	1–14	12	4	5	2	23	2.6
	15–31	19	4	3		26	1.2
	32–80	20	3	3		26	0.8

Table 7.2.1.2 Flax crop yield

Treatment	Yield (% check)			n	Mean yield (% untreated check)
	>100%	100%	<100%		
50 g tepraloxydim/ha + 0.62% v/v Dash HC	10	0	2	12	216
100 g tepraloxydim/ha + 1.24% v/v Dash HC	15	0	4	19	231

7.2.2 Equinox EC + Dash HC in dry peas

Equinox EC is proposed for use as a postemergent herbicide applied when dry peas are from emergence to the 9-leaf stage at a maximum rate (1×) of 0.25 L/ha (50 g a.i./ha) + Dash HC at 0.62% v/v.

Sixteen (16) trials conducted across the Prairie Provinces over three years using seven varieties reported crop tolerance of dry peas following application of Equinox EC.

The crop tolerance data indicated that dry peas provided acceptable crop tolerance to the application of Equinox EC + Dash HC at the maximum requested rate and the 2× rate (Table 7.2.2.1). The crop yield data indicates the application of Equinox EC + Dash HC at the maximum requested rate and 2× rate provides increased yields compared to the untreated check (Table 7.2.2.2).

Based on an assessment of the crop tolerance and yield data provided in support of dry peas, this crop is acceptable to appear on the Equinox EC label at the maximum requested rate of 50 g a.i./ha + Dash HC at 0.62% v/v.

Table 7.2.2.1 Crop tolerance of dry peas to applications of tepraloxydim + Dash HC

Treatment	DAT	0% Crop damage	<5% Crop damage	5–10% Crop damage	>10% Crop damage	n	Mean
50 g tepraloxydim/ha + 0.62% v/v Dash HC	1–14	2	6		1	10	4.9
	15–31	5	4		1	10	3.7
	32–80	7	4		0	11	0.7
100 g tepraloxydim/ha + 1.24% v/v Dash HC	1–14	4	4	1	0	9	2.2
	15–31	7	3			10	0.5
	32–80	4	5			9	2

Table 7.2.2.2 Dry peas crop yield

Treatment	Yield (% check)			n	Mean yield (% untreated check)
	>100%	100%	<100%		
50 g tepraloxydim/ha + 0.62% v/v Dash HC	5	0	1	6	191
100 g tepraloxydim/ha + 1.24% v/v Dash HC	5	0	0	5	217

7.2.3 Equinox EC + Dash HC in lentils

Equinox EC is proposed for use as a postemergent herbicide applied when lentils are from emergence to the 9-leaf stage at a maximum rate (1×) of 0.25 L/ha (50 g a.i./ha) + Dash HC at 0.62% v/v.

Thirteen (13) trials conducted across the Prairie Provinces over four years using three varieties reported crop tolerance of lentils following application of Equinox EC.

The crop tolerance data provided indicated that lentils provide acceptable crop tolerance to the application of Equinox EC + Dash HC at the maximum requested rate and the 2× rate (Table 7.2.3.1). The crop yield data indicates the application of Equinox EC + Dash HC at the maximum requested rate and the 2× rate provides increased yields compared to the untreated check (Table 7.2.3.2).

Based on an assessment of the crop tolerance and yield data provided in support of lentils, this crop is acceptable to appear on the Equinox EC label at the maximum requested rate of 50 g a.i./ha + Dash HC at 0.62% v/v.

Table 7.2.3.1 Crop tolerance of lentils to applications of tepraloxydim + Dash HC

Treatment	DAT	0% Crop damage	<5% Crop damage	5–10% Crop damage	>10% Crop damage	n	Mean
50 g tepraloxydim/ha + 0.62% v/v Dash HC	1–14	7	2		1	10	3.5
	15–31	8		2		10	1.2
	32–80	12				12	0
100 g tepraloxydim/ha + 1.24% v/v Dash HC	1–14	4	1	1		6	1.6
	15–31	4	1		1	6	2.8
	32–80	7				7	0

Table 7.2.3.2 Lentils crop yield

Treatment	Yield (% check)			n	Mean yield (% untreated check)
	>100%	100%	<100%		
50 g tepraloxydim/ha + 0.62% v/v Dash HC	5	0	1	6	198
100 g tepraloxydim/ha + 0.41% v/v Dash HC	6	0	0	6	302

7.2.4 Equinox EC + Dash HC + Buctril M (MCPA + bromoxynil) in flax

Thirteen (13) trials conducted over three years at nine locations across the Prairie Provinces using five varieties reported crop tolerance of flax following application of the tank mix of Equinox EC at 33 g a.i./ha + Dash HC at 0.41% v/v + Buctril M at 560 g a.i./ha. Nine (9) trials conducted s over two years at seven locations cross the Prairie Province using five varieties a reported crop tolerance of flax following application of the tank mix of Equinox EC at 50 g a.i./ha + Dash HC at 0.62% v/v + Buctril M at 560 g a.i./ha.

The crop tolerance data provided indicated that flax provides acceptable crop tolerance to the application of the tank mixture of Equinox EC + Dash HC + Buctril M at the requested rates. The data also indicated that, with the application of higher than requested rates crop injury, does increase slightly compared to the requested rate but is still acceptable (Table 7.2.4.1). The crop yield data provided indicated the application of the Equinox EC + Dash HC + Buctril M tank mixture at the requested rates, and higher rates, provides increased yields compared to the untreated check (Table 7.2.4.2).

Based on an assessment of the crop tolerance and yield data provided in support of the tank mixture of Equinox EC + Dash HC + Buctril M, this tank mix is acceptable to appear on the Equinox EC label at the requested rates.

Table 7.2.4.1 Crop tolerance of flax to applications of tepraloxydim + Dash HC + Buctril M

Treatment	DAT	0% Crop damage	<5% Crop damage	5–10% Crop damage	>10% Crop damage	n	Mean
33 g tepraloxydim/ha + 0.41% v/v Dash HC + 560 g a.i./haBuctril M	1–14	3	6	3		12	2.6
	15–31	8	4			12	0.6
	32–80	8	2	2		12	1.4
50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	1–14	1	6	1		8	2.6
	15–31	5	3			8	1.1
	32–80	3	4	1		8	1.8
66 g tepraloxydim/ha + 0.82% v/v Dash HC + 1120 g a.i./ha Buctril M	1–14	1		1	2	4	12.3
	15–31	1		1	2	4	8.4
	32–80	2	1	1		4	2.5

Table 7.2.4.2 Flax crop yield

Treatment	Yield (% check)			n	Mean yield (% untreated check)
	>100%	100%	<100%		
33 g tepraloxydim/ha + 0.41% v/v Dash HC + 560 g a.i./ha Buctril M	8	0	2	10	229
50 g tepraloxydim/ha + 0.62% v/v Dash HC + 560 g a.i./ha Buctril M	6	0	0	6	228
66 g tepraloxydim/ha + 0.82% v/v Dash HC + 1120 g a.i./ha Buctril M	3	0	1	4	347

7.2.5 Equinox EC + Dash HC + Flaxmax (MCPA + clopyralid) in flax

Eight (8) trials conducted in one year at seven locations across the Prairie Provinces using two varieties reported crop tolerance of flax following application of the tank mix of Equinox EC at 33 g a.i./ha + Dash HC at 0.41% v/v + Flaxmax at 660 g a.i./ha. Nine (9) trials conducted over two years at seven locations across the Prairie Provinces using five varieties reported crop tolerance of flax following application of the tank mix of Equinox EC at 50 g a.i./ha + Dash HC at 0.62% v/v + Flaxmax at 660 g a.i./ha.

The crop tolerance data provided indicated that flax provides acceptable crop tolerance to the application of the tank mixture of Equinox EC + Dash HC + Flaxmax at the requested rates. The data also indicated that, with the application of higher than requested rates, crop injury does increase slightly compared to the requested rates but is still acceptable (Table 7.2.5.1). The crop yield data provided indicates that the application of the

Equinox EC + Dash HC + Flaxmax tank mixture at the requested rate and higher rates provides increased yields compared to the untreated check (Table 7.2.5.2).

Based on an assessment of the crop tolerance and yield data provided in support of the tank mixture of Equinox EC + Dash HC + Flaxmax, this tank mix is acceptable to appear on the Equinox EC label at the requested rates.

Table 7.2.5.1 Crop tolerance of flax to applications of tepraloxydim + Dash HC + Flaxmax

Treatment	DAT	0% Crop damage	<5% Crop damage	5–10% Crop damage	>10% Crop damage	n	Mean
33 g tepraloxydim/ha + 0.41% v/v Dash HC + 660 g a.i./ha Flaxmax	1–14	1	1	3	1	6	6.2
	15–31	3	5			8	1.5
	32–80	5	2	1		8	0.9
50 g tepraloxydim/ha + 0.62% v/v Dash HC + 660 g a.i./ha Flaxmax	1–14	3	3	2		8	2.5
	15–31	6	1	1		8	0.8
	32–80	6	1	1		8	1.1
66 g tepraloxydim/ha + 0.82% v/v Dash HC + 1320 g a.i./ha Flaxmax	1–14	0	1	1	6	8	16.5
	15–31	1	1	4	2	8	8.2
	32–80	1	6	1		8	2.7

Table 7.2.5.2 Flax crop yield

Treatment	Yield (% check)			n	Mean yield (% untreated check)
	>100%	100%	<100%		
33 g tepraloxydim/ha + 0.41% v/v Dash HC+ 660 g a.i./ha Flaxmax	6		1	7	260
50 g tepraloxydim/ha + 0.62% v/v DashHC + 660 g a.i./ha Flaxmax	5		1	6	229
66 g tepraloxydim/ha + 0.82% v/v Dash HC + 1320 g a.i./ha Flaxmax	5	1	1	7	260

7.3 Observations on undesirable or unintended side effects

7.3.1 Impact on succeeding crops

ACCase products undergo rapid photodegradation in water and soil as well as being subject to microbial degradation. The short half-life that results gives this group of herbicides little residual activity and no crop rotation limitations the year following application (Table 7.3.1.1).

Table 7.3.1.1 Crop rotation recommendations for registered ACCase Herbicides

Herbicide	Restrictions year after application*
Sethoxydim	None
Clethodim	None
Tralkoxydim	None
Quizalofop	None
Diclofop	None
Fluazifop	None
Fenoxaprop	None
Clodinafop	None

* Respective label information

Five (5) studies, each consisting of two trials, tested the effect of tepraloxydim in plantback studies at 0 DAT, one week after treatment (WAT), two WAT and four WAT on field corn, sorghum, Sudan grass and red rice (tables 7.3.1.2 through 7.3.1.6).

There was a consistent response of the various grassy crops to the application of Equinox EC applied prior to planting. When the crop was planted 0 and 7 DAT, the higher than requested rates of Equinox EC of 100 g a.i./ha (2× maximum) and 200 g a.i./ha (4× maximum) did result in visual injury for all of the crops. However, when the crops were planted 14 and 28 DAT, there was very little injury even at the higher rates of 100 g a.i./ha and 200 g a.i./ha.

Results indicate that for the maximum requested rate of 50 g a.i./ha, when the crops are planted 7–14 DAT there is little or no visual injury.

These data confirm the rationale that Equinox EC has little or no soil activity and is similar to other ACCase products.

Based on the above, a minimum of 14 days will be required between application of Equinox EC and the replanting of cereal or grass crops. A cultivation to a minimum depth of 10 cm is recommended seven days prior to seeding. No other crop rotation restrictions are necessary.

Table 7.3.1.2 Crop injury reported for field corn planted 0, 7, 14 and 28 days after treatment of various rates of tepraloxydim—trial 1

Tepraloxydim g a.i./ha	Crop planted 0 days after treatment	Crop planted 7 days after treatment	Crop planted 14 days after treatment	Crop planted 28 days after treatment
Field corn: Visual rating taken 20 days after planting				
50	3	0	0	0
100	22	1	0	0
200	42	7	0	0
Field corn: Visual rating taken 35 days after planting				
50	2	0	1	0
100	3	0	1	0
200	10	2	1	0

Table 7.3.1.3 Crop injury reported for Sudan grass planted 0, 7, 14 and 28 days after treatment of various rates of tepraloxydim—trial 2

Tepraloxydim g a.i./ha	Crop planted 0 days after treatment	Crop planted 7 days after treatment	Crop planted 14 days after treatment	Crop planted 28 days after treatment
Sudan grass: Visual rating taken 20 days after planting				
50	27	3	0	0
100	62	11	5	0
200	84	50	2	2
Sudan grass: Visual rating taken 35 days after planting				
50	11	0	10	0
100	26	3	10	0
200	49	23	2	0

Table 7.3.1.4 Crop injury reported for red rice planted 0, 7, 14 and 28 days after treatment of various rates of tepraloxydim—trial 3

Tepraloxydim g a.i./ha	Crop planted 0 days after treatment	Crop planted 7 days after treatment	Crop planted 14 days after treatment	Crop planted 28 days after treatment
Red rice: Visual rating taken 7–8 days after planting				
50	0	0	0	0
100	10	3	0	0
200	45	10	3	0
Red rice: Visual rating taken 18–20 days after planting				
50	7	0	0	0
100	45	10	0	0
200	90	15	0	0
Red rice: Visual rating taken 28–34 days after planting				
50	0	0	0	0
100	33	0	0	0
200	50	0	0	0

Table 7.3.1.5 Crop injury reported for sorghum planted 0, 7, 14 and 28 days after treatment of various rates of tepraloxydim—trial 4

Tepraloxydim g a.i./ha	Crop planted 0 days after treatment	Crop planted 7 days after treatment	Crop planted 14 days after treatment	Crop planted 28 days after treatment
Sorghum: Visual rating taken 7–8 days after planting				
50	2	0	0	0
100	4	0	0	0
200	32	0	0	0
Sorghum: Visual rating taken 18–20 days after planting				
50	8	7	0	0
100	10	10	0	0
200	44	26	1	0
Sorghum: Visual rating taken 28–34 days after planting				
50	5	3	1	0
100	11	9	1	0
200	30	22	1	1

Table 7.3.1.6 Crop injury reported for field corn planted 0, 7, 14 and 28 days after treatment of various rates of tepraloxydim—trial 5

Tepraloxydim g a.i./ha	Crop planted 0 days after treatment	Crop planted 7 days after treatment	Crop planted 14 days after treatment	Crop planted 28 days after treatment
Field corn: Visual rating taken 7–8 days after planting				
50	0	0	0	0
100	0	0	0	0
200	0	0	0	0
Field corn: Visual rating taken 18–20 days after planting				
50	2	0	0	0
100	3	0	0	0
200	3	7	2	0
Field corn: Visual rating taken 28–34 days after planting				
50	2	0	0	0
100	2	0	0	0
200	3	7	1	0

7.4 Economics

Flax, dry peas and lentils are major crops grown in Canada. Table 7.4.1 presents the production of each crop for the year 2000. Yield losses due to grass weed infestation can be significant. Table 7.4.2, which was provided by the applicant, presents potential flax yield losses caused by various grass weeds at various densities.

The need to control grass weed species in flax, dry peas and lentils in western Canada is essential in order to maximize yields and minimize seed dockage at harvest.

Table 7.4.1 Production of flax, dry peas and lentils in Canada in the year 2000

Crop	Production (tons)
Flax	694 000
Dry Peas	2 864 000
Lentils	914 000

Table 7.4.2 Potential yield losses (percent) of grass weeds in flax

Weed	Weed density—Number per metre squared				
	2	20	30	50	200
Foxtail	NA	NA	NA	3% loss	10% loss
Volunteer Barley	12% loss	21% loss	28% loss	34% loss	39% loss
Volunteer Wheat	11% loss	18% loss	24% loss	29% loss	33% loss
Wild Oats	8% loss	12% loss	15% loss	17% loss	19% loss

7.5 Sustainability

7.5.1 Survey of alternatives

7.5.1.1 Non-chemical control practices

Non-chemical means of weed control include cultivation and crop rotation. The postemergent use of Equinox EC would not exclude the use of cultivation. There are no recropping restrictions allowing flexibility in selecting crops to be planted the year after application.

7.5.1.2 Chemical control practices

Application of Equinox EC would not exclude the sequential use of other herbicides with different modes of action for control of annual and perennial weeds not controlled by the product alone or when tank mixed.

There are numerous grass and broadleaf weed herbicides, with different modes of action, that may be used alone or in various tank mix combinations for use in flax, dry peas and lentils (Table 7.5.1.2.1).

Table 7.5.1.2.1 Herbicides registered for use on flax, lentils and dry peas in Canada

Herbicide	Weed resistance group	Flax	Lentils	Dry Peas
Assure	1	x	x	x
Avadex	8	x		x
Edge	3		x	x
Fusion	1	x	x	x
Odyssey	2			x
Poast Ultra	1	x	x	x
Pursuit	2			x
Select	1	x	x	x
Trifluralin	3	x	x	x
Venture	1	x	x	x

7.5.2 Contribution to risk reduction

Equinox EC alone will provide control of certain grass weeds at a low amount of active ingredient per hectare.

7.5.3 Information on the occurrence or possible occurrence of the development of resistance

To address the issue of development of herbicide resistance, the label includes the resistance-management statement as outlined in Regulatory Directive DIR99-06 entitled *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action* as follows.

> HERBICIDE RESISTANCE MANAGEMENT:
>
> For resistance management, tepraloxydim is a Group 1 herbicide. Any weed population may contain or develop plants naturally resistant to this and other Group 1 herbicides. The resistant biotypes may dominate the weed population if these herbicides are used repeatedly in the same field. Other resistance mechanisms that are not linked to site of action, but specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance-management strategies should be followed.

To delay herbicide resistance:

- Where possible, rotate the use of Group 1 herbicides with different herbicide groups that control the same weeds in a field.
- Use tank mixtures with herbicides from a different group when such use is permitted.
- Herbicide use should be based on an integrated pest management (IPM) program that includes scouting, historical information related to herbicide use and crop rotation, and considers tillage (or other mechanical), cultural, biological and other chemical control practices.
- Monitor treated weed populations for resistance development.
- Prevent movement of resistant weed seeds to other fields by cleaning harvesting and tillage equipment and planting clean seed.
- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance-management and/or integrated weed-management recommendations for specific crops and weed biotypes.
- For further information or to report suspected resistance, contact BASF representative or call BASF toll-free at 1-800-253-4536.

7.6 Conclusions

Tepraloxydim is formulated in one end-use product. Equinox EC herbicide is an emulsifiable concentrate formulation with a guarantee of 200 g/L of tepraloxydim that must be applied with the adjuvant Dash HC.

Equinox EC is a selective herbicide for use as a postemergence application to flax (including low linolenic acid and sulfonyl urea tolerant varieties), lentils and dry peas grown in the Prairie Provinces and the Peace River Region of British Columbia for the control of specific grass weeds. Equinox EC must be applied with Dash HC adjuvant at 0.41–0.62% v/v (i.e., 0.41 L Dash HC/100 L spray solution) in a spray volume of 100 L/ha with a maximum of one application per year using ground equipment only.

There are two proposed rates of application for Equinox EC. Equinox EC applied at a rate of 0.165 L/ha (33 g a.i./ha) plus Dash HC adjuvant at 0.41% v/v is effective for the control of wild oats (*Avena fatua*), green foxtail (*Setaria viridis*), volunteer barley (*Hordeum vulgare*) and volunteer wheat (*Triticum aestivum*) at the 1–6 leaf stage up to two tillers. Equinox EC applied at a rate of 0.250 L/ha (50 g a.i./ha) plus Dash HC adjuvant at 0.62% v/v is effective for the control of quackgrass (*Agropyron repens*) at the 3–6 leaf stage as well as the above listed annual grass weeds when weed densities are

high and overlapping, when staging is late or when weeds are under stress and not growing as actively due to moisture or temperature stress.

There are no rotational cropping restrictions necessary for Equinox EC.

Proposed tank mixes with Equinox EC plus Dash HC adjuvant include Buctril M (MCPA + bromoxynil) at 1.0 L/ha or Flaxmax (MCPA + clopyralid) at 2.0 L/ha when applied to flax.

8.0 Toxic Substances Management Policy considerations

During the review of tepraloxydim, the PMRA has considered the implications of the Toxic Substances Management Policy (TSMP) and PMRA Regulatory Directive DIR99-03 and has concluded the following:

> Tepraloxydim does not meet the TSMP criteria for persistence in soil under aerobic and anaerobic water/soil systems. The half-life values of tepraloxydim in soil (5.3 days), in anaerobic water/soil systems (9 days) and in aerobic water/sediment systems (171.4 days) are below the TSMP Track 1 cut-off criteria for soil (182 days). No data were provided for tepraloxydim persistence in air but tepraloxydim is not expected to volatilize.
>
> Tepraloxydim is not bioaccumulative. The octanol–water partition coefficient (log K_{ow}) of tepraloxydim is 1.5, which is below the TSMP Track-1 cut-off criterion of 5.0.
>
> Tepraloxydim does not meet the criteria of the *Canadian Environmental Protection Act* (CEPA) for CEPA-toxic or CEPA-toxic equivalent under the TSMP.
>
> Tepraloxydim forms two transformation products DP-1 and DP-2, under field conditions. DP-1 is non-persistent (DT_{50} = 28 days) and does not meet the TSMP Track 1 criteria of greater than 180 days for persistence. DP-2 is persistent in soils (DT_{50} = 198-235 days) and meets the TSMP Track 1 criteria for persistence (DT_{50} >180 days).
>
> Tepraloxydim does not contain any byproducts or microcontaminants that meet the TSMP Track 1 criteria. Impurities of toxicological concerns are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process. The formulated product does not contain any formulants that are known to contain TSMP Track 1 substances.

9.0 Proposed regulatory decision

9.1 Proposed regulatory decision

The PMRA has carried out an assessment of available information in accordance with Section 9 of the Pest Control Products (PCP) Regulations and has found it sufficient pursuant to Section 18(*b*), to allow a determination of the safety, merit and value of technical grade tepraloxydim, Equinox EC end-use product and Dash HC adjuvant manufactured by BASF. The Agency has concluded that the use of tepraloxydim technical, Equinox EC end-use product and Dash HC adjuvant in accordance with the label has merit and value consistent with section 18(*c*) of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18(*d*). Therefore, based on the considerations outlined above, the use of tepraloxydim technical, Equinox EC end-use product and Dash HC adjuvant for the control of annual and perennial grasses in flax, lentils and dry peas are proposed for full registration, pursuant to Section 13 of the PCP Regulations.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

9.2 Additional data requirements

NA

List of abbreviations

ACCase	acetyl CoA carboxylase
AD	administered dose
ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
BCF	bioconcentration factor
bw	body weight
bwg	body-weight gain
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
DAT	day(s) after treatment
DFR	dislodgeable foliar residue
DT_{50}	time required to dissipate 50% of the original concentration
DT_{90}	time required to dissipate 90% of the original concentration
dw	dry weight
EC_{50}	concentration or application rate at which 25% effects are observed
ECD	electron capture detection
EEC	expected environmental concentration
ELCD-N	electrolytic conductivity detection in nitrogen
ELCD-X	electrolytic conductivity detection in halogen
EP	end-use product
FC	food consumption
GC	gas chromatography
GC/MS	gas chromatography/mass spectography
HDPE	high-density polyethylene
HPLC	high-performance liquid chromatography
IPM	integrated pest management
IUPAC	International Union of Pure and Applied Chemistry
IV	intravenous
K_{ow}	octanol–water partition coefficient
L	litre
LC	liquid chromatrography
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LER	lowest effective rate
LOAEL	lowest observed adverse effect level
LOQ	limit of quantitation
MCPA	4-chloro-2-methylphenoxyacetic acid
MIS	mean irritation score
MMAD	mass median aerodynamic diameter
MOS	margin of safety
MRL	maximum residue limit
MRM	Multiresidue Method

MS	mass spectrometry
MTD	maximum tolerated dose
MTDB	maximum theoretical dietary burden
NA	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NPD	nitrogen-phosphorus detection
NZW	New Zealand white
PAM	Pesticide Analytical Manual
PBI	plantback inerval
PCP	pest control product
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
PII	primary irritation index
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
PRDD	Proposed Regulatory Decision Document
RAC	raw agricultural commodity
ROC	residue of concern
RQ	risk quotient
T½	half-life
TC	transfer coefficient
T_{max}	time to reach maximum concentration
TGAI	technical grade active ingredient
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UDS	unscheduled DNA synthesis
UF	uncertainty factor
U.S.	United States
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
UV	ultraviolet
WAT	week(s) after treatment

Appendix I Toxicology

METABOLISM—Tepraloxydim and 5-OH-tepraloxydim

In pharmacokinetics metabolism studies in male and female rats, tepraloxydim was readily and almost completely absorbed after oral and IV administration. The peak plasma levels were attained within 0.5 to 2 h of dosing. The plasma half-life of radiolabelled tepraloxydim is 4–10 h. Excretion was rapid, mainly via the urine (65–80%), while fecal elimination comprised 16–25% of the administered dose (AD). Total recovery was 94–101% within 48 h. Excretion was 2–3 fold higher in the bile than the feces, suggesting enterohepatic recirculation. No accumulation of radioactivity was observed in any tissue at 120 h postdosing. The biotransformation of tepraloxydim in rats resulted in a large number of metabolites in urine, feces and bile. The main metabolic pathway was the oxidation at the pyran ring to the lactone via a hydroxy metabolite and cleavage of the oxime ether group with the imine and oxazol as products. At near plasma T_{max} (1 h postdosing), the parent compound was the main product in the plasma, liver and kidneys. As well, the parent compound constituted 16–34% of the urinary residues, 1–2% of the fecal residue and 8–11% of the residues in the bile. The results indicate that absorption, distribution, metabolism and excretion of tepraloxydim are independent from dose levels, route of administration and sex.

Metabolism of 5-OH-tepraloxydim in male and female Wistar rats indicated that absorption was rapid and virtually complete. Radioactivity was distributed in all tissues and organs throughout the body, but by 120 h, tissue radioactivity was below 1 ppm, indicating low tissue accumulation. Excretion of orally and intravenously administered radioactivity was rapid and was mainly via the urine, accounting for 66–82% AD, while fecal excretion of radioactivity accounted for 18–29% AD. Biliary excretion amounted to about 20–26% AD. No radioactivity was detected in exhaled air. Total recovery was 93.3–100% within 48 h. Plasma clearance kinetics revealed peak whole blood and plasma concentration at 0.5–2.0 h regardless of the dose. There was no biologically relevant gender-related or dose-related differences in absorption, distribution, metabolism and excretion of 5-OH-tepraloxydim. Identification of metabolites was not investigated in this study. The information was available in a separate study, but the report was not submitted to the PMRA for evaluation.

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
ACUTE STUDIES—technical active (code name Reg. No. 191 819)			
Oral—rat	**Reg. No. 191 819**, N32, 95%, rat, Wistar, 5/sex/group 464, 2000, or 5000 mg/kg bw	LD_{50} ♂♀ >2000 mg/kg bw **Low toxicity**	mortality: 5000 ppm—3♂, 2♀; within 2 days clinical signs: 5000: ♂♀—impaired/poor general state, dyspnoea, staggering, apathy, piloerection, salivation, tremor, twitching, compulsory gnawing, splastic gait, exsiccosis, discoloured urine, red snout/eye 2000: ♂—salivation; ♀—poor general state, dyspnoea, staggering, apathy, piloerection, salivation, red snout normal by day 2 bw: all survivors gained weight gross pathology: decedents—general congestion and bloody content of GI tract, stomach erosion terminal sacrifice—no abnormalities
Dermal—rat	**Reg. No. 191 819**, N32, 94.95%, rat, Wistar, 5/sex 2000 mg/kg bw in distilled water	LD_{50} ♂♀ >2000 mg/kg bw **Low toxicity**	no mortality, no effects on clinical signs or gross pathology at terminal sacrifice normal bwg
Inhalation—rat 4 h head/nose-only exposure	**Reg. No. 191 819**, N32, 94.95%, rat, Wistar, 5/sex 5.1/23.0 mg/L (actual/nominal concentration)	MMAD ± GSD = 1.8 µm ± 3.1; 60% particles ≤2.6 µm LC_{50} ♂♀ > 5.1 mg/L **Low toxicity**	no mortality, no effects on bw and gross pathology non-specific clinical signs during exposure; normal by day 1
Eye irritation—rabbit	**Reg. No. 191 819**, N32, 94.95%; 0.1 g/eye rabbit, White Vienna, 2♂ + 4♀	Maximum mean score at 1 h = 9/110 **Minimally irritating**	mean irritation scores (MIS): at 1, 24, 48, 72 h = 9, 1, 0, 0 (maximum = 110), respectively, primary irritation index (PII) = 0.3/110
Skin irritation (4 h)—rabbit	**Reg. No. 191 819**, N32, 94.95%, 0.5 g/rabbit rabbit, White Vienna, 2♂ + 4♀	Maximum mean score = 0/8 **Non-irritating**	no skin reactions except grade 1 erythema at one test skin site at 1 h

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Dermal sensitization—guinea pig (Maximization test)	**Reg. No. 191 819**, N32, 94.95%, guinea pig, Pirbright White Dunkin Hartley, 20 ♀ in test, 10 ♀ in control	induction injections with 5% Reg. No. 191 819; percutaneous induction—50% aqueous test material; percutaneous challenge—25% aqueous test material; separate positive control study (1-chloro-2,4-dinitrobenzol, DNCB)	induction injection: grade 2 erythema/edema percutaneous induction: grade 2 erythema/edema percutaneous challenge: no skin reaction **Not a skin sensitizer**
ACUTE STUDIES—5-OH-tepraloxydim (code name Reg. No. 275 522; a metabolite of tepraloxydim)			
Oral—rat	**Reg. No. 275 522**, 00448-1, 91.3%, rat, Wistar, 5/sex/group 2000, 3000, 5000 mg/kg bw	LD_{50} ♂♀ >5000 mg/kg bw **Low toxicity**	no mortality: all rats gained weight clinical signs: non-specific signs—poor/impaired general state, dyspnea, apathy, staggering and/or erythema 2000 mg/kg bw—no clinical signs in ♀ bw: all survivors gained weight gross pathology: no abnormalities
ACUTE STUDIES—Equinox EC Herbicide (code name BAS 620 00 H, containing 20.5% tepraloxydim)			
Oral—rat	**BAS 620 00 H**, 94-4 rat, Wistar, 5/sex/group, 2000, 3000, 5000 mg/kg bw	LD_{50} ♂♀ > 2000 mg/kg bw **Low toxicity**	mortality: 5000—all ♂♀ (all deaths within 2 d 3000—4♂, all ♀ of dosing) clinical signs: impaired/poor general state, dyspnea, apathy, abdominal or lateral position, staggering, tremor, paresis, piloerection, exsiccosis, salivation, red clammy snout/eyelids, compulsive gnawing, atonia, lacrimation, chromodacryorrhea and/or discoloured urine; survivors normal by d 9 bw: all survivors gained weight gross pathology: decedents—agonal congestion (1 high-dose ♀), discolouration of small intestine and urinary bladder (all high-dose rats except 1 ♀), erosion/ulcer of glandular stomach (high-dose—2♂, 4♀; mid-dose—4♂, 5♀) and severe congestion and focal hemorrhage of the urinary bladder (1 high-dose ♂) terminal sacrifice—no abnormalities
Dermal—rat (24 h exposure)	**BAS 620 00 H**, 94-4 rat, Wistar, 5/sex/group, 4000 mg/kg bw	LD_{50} ♂♀ >2000 mg/kg bw **Low toxicity**	no mortality, no effects on gross pathology at terminal sacrifice; normal bwg clinical signs: impaired general state, dyspnoea and cyanosis local effects: well-defined to moderate erythema, very slight to slight edema and hemorrhage
Inhalation—rat 4 h head/nose-only exposure	**BAS 620 00 H**, 94-4 rat, Wistar, 5/sex 5.4/41.3 mg/L (actual/nominal concentration)	MMAD ± GSD = 1.0 µm ± 2.47; 88% particles ≤3 µm LC_{50} ♂♀ >5.4 mg/L **Low toxicity**	no mortality, no effects on bw and gross pathology clinical signs: during exposure—exhibited irregular, accelerated, or intermittent respiration postexposure—accelerated or intermittent respiration, respiratory sound, nasal discharge, piloerection and/or smeared fur normal by day 7
Eye irritation—rabbit	**BAS 620 00 H**, 94-4 0.1 g/eye rabbit, NZW, 1♂+5♀	Maximum mean score at 24 h = 19.7/110 **Moderately irritating** **WARNING—EYE IRRITANT**	MIS (maximum = 110): at 1, 24, 48, 72 h, d 8 = 11.1, 19.7, 11.8, 6.7, 0, respectively; PII (mean of 24, 48 and 72 h scores) = 12.7/110 corneal opacity in 4/6 treated eyes within 24 h, persisted up to 72 h, with recovery by day 8; One treated eye showed loss of corneal tissue

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Skin irritation—(4 h)—rabbit	**BAS 620 00 H**, 94-4 0.5 g rabbit, NZW, 5♂+1♀	Maximum mean score = 4.2/8 **Moderately irritating** **WARNING—SKIN IRRITANT**	MIS (maximum = 8): at 1, 24, 48, 72 h, d 8, d 15 = 4, 4, 4.2, 3.8, 0.5, 0, respectively; PII (mean of 24, 48 and 72 h scores) = 4/8
Dermal sensitization—guinea pig (Buehler test)	**BAS 620 00 H**, 94-4 guinea pig, Pirbright White Dunkin Hartley, 20 ♀ in test, 10 ♀ in control separate positive control (α-hexylcinnamaldehyde)	induction: 9 each with 0.5 mL 100% test article; 6 h exposure/application challenge: 13 d after 9th induction with 0.5 mL of 75% aqueous test article	induction: very slight to well-defined erythema and/or very slight to slight edema challenge: no skin reaction **Not a skin sensitizer**
ACUTE STUDIES—Equinox EC Herbicide (code name BAS 620 00 H) + Dash HC adjuvant (1:4 ratio)			
Oral—rat	**BAS 620 00 H + Dash HC (1:4)**, 95/35/94-4; 95/227/95-2 rat, Wistar, 5/sex/group, 5000 mg/kg bw	LD_{50}, ♂♀ >5000 mg/kg bw	no deaths, no effects on bw or gross pathology clinical signs: poor/impaired general state, dyspnoea, apathy, staggering, piloerection, lacrimation, smeared fur and/or red clammy snout and/or eyelid **Low toxicity**
Dermal—rat (24 h exposure)	**BAS 620 00 H + Dash HC (1:4)**, 95/35/94-4; 95/227/95-2 rat, Wistar, 5/sex/group, 4000 mg/kg bw	LD_{50}, ♂♀ >4000 mg/kg bw **Low toxicity**	no mortality, no effects on gross pathology at terminal sacrifice; normal bwg clinical signs: non-specific signs in 1♀ local effects: well-defined to moderate erythema, very slight to slight edema and hemorrhage on d1; scaling up to 14 days
Inhalation—rat 4 h head/nose-only exposure	**BAS 620 00 H + Dash HC (1:4)**, 95/35/94-4; 95/227/95-2 rat, Wistar, 5/sex 5.3/36.7 mg/L (actual/nominal concentration)	MMAD ± GSD = 0.7 µm ± 2.71; 93% particles ≤3 µm LC_{50}, ♂♀ >5.3 mg/L **Low toxicity**	no mortality, no effects on bw and gross pathology clinical signs: attempts to escape, signs of irritation to respiratory tract, squatting posture, piloerection and smeared fur; normal by d 5
Eye irritation—rabbit	**BAS 620 00 H + Dash HC (1:4)**, 95/35/94-4; 95/227/95-2 0.1 mL/eye rabbit, NZW, 1♂ + 5♀	Maximum mean score at 24 h = 19.7/110 **Mildly irritating**	MIS (maximum = 110): at 1, 24, 48, 72 h, d 8, d 15 = 12.0, 21.7, 13.8, 7.3, 0.7, 0, respectively; PII (mean of 24, 48 and 72 h scores) = 14.3/110
Skin irritation—(4 h)—rabbit	**BAS 620 00 H + Dash HC (1:4)**, 95/35/94-4; 95/227/95-2 0.5 mL rabbit, NZW, 5♂ + 1♀	Maximum mean score = 5/8 **Moderately irritating**	MIS (maximum = 8): at 1, 24, 48, 72 h, d 8, d 15 = 5, 4.67, 4.33, 4, 1.5, 1.17, respectively; PII (mean of 24, 48 and 72 h scores) = 4.3/8
Dermal sensitization—guinea pig (Buehler test)	**BAS 620 00 H + Dash HC (1:4)**, 95/35/94-4; 95/227/95-2 guinea pig, Pirbright White Dunkin Hartley, 20 ♀ in test, 10 ♀ in control	induction: 9 each with 0.5 mL 50% aqueous test article; 6 h exposure/application challenge: 13 d after 9th induction with 0.5 mL of 25% aqueous test article separate positive control (α-hexylcinnamaldehyde)	induction: distinct erythema and edema challenge: no skin reaction **Not a skin sensitizer**

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
ACUTE STUDIES—Dash HC adjuvant (Code name BCH 815 25 S)			
Oral—rat	**BCH 815 25 S**, F9001 rat, Wistar, 5/sex/group, 2200 mg/kg bw	LD_{50}, ♂♀ >2200 mg/kg bw **Low toxicity**	no deaths; no effects on bw or gross pathology clinical signs: impaired general state, apathy, blood crusted snout and/or piloerection
Dermal—rat (24 h exposure)	**BCH 815 25 S**, F9001 rat, Wistar, 5/sex/group, 2000 mg/kg bw	LD_{50}, ♂♀ >2000 mg/kg bw **Low toxicity**	no mortality or clinical signs, no effects on gross pathology bw: ♀ lost weight during week 1, normal bwg at study termination local effects: erythema
Inhalation—rat 4 h head/nose-only exposure	**BCH 815 25 S**, F9001 rat, Wistar, 5/sex/group 1.3 or 5.6 mg/L (actual) 2.77 or 16.6 mg/L (nominal)	MMAD ± GSD = 1.6 µm ± 4.7; 84% particles ≤ 5.5 µm LC_{50}, ♂♀ >5.6 mg/L **Low toxicity**	no mortality, no effects on bw or gross pathology clinical signs: during and within 24 h after exposure irregularity of respiration (intermittent, irregular, accelerated and/or respiratory sounds), reddish eye discharge, squatting position, nose with reddish smear and crusts, ruffled fur and/or urine-contaminated fur
Eye irritation— rabbit	**BCH 815 25 S**, F9001 0.1 mL/eye rabbit, White Vienna, 4♂ + 2♀	Maximum mean score at 24 h = 27/110 **Moderately irritating** **WARNING— EYE IRRITANT**	MIS (maximum = 110): at 1, 24, 48, 72 h, d 8, d 15, d 21 = 11.3, 27.0, 23.7, 22.5, 4.7, 3.8, 2.3, respectively; PII (mean of 24, 48 and 72 h scores) = 24.4/110
Skin irritation— (4 h)—rabbit	**BCH 815 25 S**, F9001 0.5 mL rabbit, White Vienna, 4♂ + 2♀	Maximum mean score = 3.5/8 **Moderately irritating** **WARNING— SKIN IRRITANT**	MIS (maximum = 8): at 1, 24, 48, 72 h, d 8, d 15 = 2.5, 2.67, 3.5, 3.5, 1.0, 0, respectively; PII (mean of 24, 48 and 72 h scores) = 3.5/8
Dermal sensitization— guinea pig (maximization test)	**BCH 815 25 S**, F9001 guinea pig, Pirbright White Dunkin Hartley, 20 ♀ in test, 10 ♀ in each of negative control separate positive control, DNBC	induction injections: 0.1 mL with or without Freund's complete adjuvant percutaneous induction: 3 wk after intradermal induction—0.3 g of 25% aqueous test material; 48 h exposure percutaneous challenge: 21 d later percutaneous induction—0.15 g of 10% aqueous test material	intradermal induction: distinct erythema and edema percutaneous induction: distinct edema, necrotic challenge: slight erythema was observed in 1/20 **Not a skin sensitizer**
SHORT TERM—Tepraloxydim technical (code name Reg. No. 191 819) and 5-OH-tepraloxydim (code name Reg. No. 275 522)			
28-day dietary— mouse	**Reg. No. 191 819** N19, 97.3%; mouse, B6C3F1 Cr1Br (VAF), 5/sex/group 0, 500, 2000, 5000, 7500 ppm (♂ = 0, 123, 506, 1518, 2608; ♀ = 0, 161, 664, 2259, 4227 mg/kg bw/d)	NOAEL ♂♀ = 2000 ppm ♂ = 506, ♀ = 664 mg/kg bw/d LOAEL ♂♀ = 5000 ppm ♂ = 1518, ♀ = 2259 mg/kg bw/d	no deaths, no clinical signs of toxicity food intake: no apparent treatment-related findings, but highly variable in high-dose mice, especially ♀ resulting in unreliable values on test compound intake 7500 ppm: ♂♀—↓ bw; ↑ rel liver and kidney wt; fatty change in renal proximal tubular cells ♂—bw loss; ↓ RBC, Hb, Hct; hepatocellular hypertrophy; 5000 ppm: ♂♀—↓ bw; ♂—hepatocellular hypertrophy

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
28-day dietary—rat	**Reg. No. 191 819** N19, 97.3%; rat, Wistar Chbb:THOM (SPF), 5/sex/group 0, 500, 5000, 7500, 10000 ppm (♂ = 0, 46, 469, 682, 929; ♀ = 0, 49, 489, 732, 954 mg/kg bw/d)	NOAEL: ♂♀ = 500 ppm ♂ = 46, ♀ = 49 mg/kg bw/d LOAEL: ♂♀ = 5000 ppm ♂ = 469, ♀ = 89 mg/kg bw/d based on lower bw and bwg	no deaths; no effects on food efficiency, hematology, neurological functions, or gross pathology 10 000 ppm: ♂♀—↓ bw, bwg, food intake; ↑ water intake; ↑ total bilirubin, creatinine ♂—↓ bone marrow cellularity, liver centrilobular hepatocyte hypertrophy; kidney hyaline droplet degeneration ♀—urine-smeared anogenital region (2) 75 000 ppm: ♂♀—↓ bw, bwg, food intake; urine-smeared anogenital region(1♂, 2♀); ↑ total bilirubin, creatinine ♂—liver centrilobular hepatocyte hypertrophy; kidney hyaline droplet degeneration 5000 ppm: ♂—↓ bw, bwg; liver centrilobular hepatocyte hypertrophy; renal hyaline droplet degeneration
28-day dietary—dog	**Reg. No. 191 819** N19, ~97.3%; dog, beagle; 2/sex/group 0, 1000, 4000, 8000, 10 000 ppm (♂ = 0, 30, 120, 228, 324; ♀ = 0, 32, 126, 246, 376 mg/kg bw/d)	NOAEL not determined LOAEL not determined	no deaths; no effects on clinical signs, bw, 10 000 ppm: ♂—↓ food intake, bwg, food efficiency (1♂) possible treatment-related effects: ♂♀—↑ abs and rel wt of liver (≥4000 ppm); centrilobular hepatic hypertrophy (1♂, 2♀) ♂—↓ abs and rel wt of epididymides and testes (1 each at 1000, 4000 ppm; both ♂ at 8000 and 12 000 ppm); ↓ testis size (1 each at 1000, 4000, 12 000 ppm) testes—minimal tubular degeneration, minimal multifocal reduced thickness of the germinal epithelium and intratubular giant cells (1 each at 4000 and 12 000 ppm) small group size and highly variable values on most assessed parameters did not permit a meaningful assessment of the toxicity potential of the test material; thus no NOAEL and LOAEL were determined.
90-day dietary—mouse	**Reg. No. 191 819** N32, 94.9%; mouse, C57BL/6N Crl BR; 10/sex/group 0, 300, 1200, 5000 ppm (♂ = 0, 82, 310, 1484; ♀ = 0, 107, 424, 1912 mg/kg bw/d)	NOAEL: ♂♀ = 1200 ppm ♂ = 310, ♀ = 424 mg/kg bw/d LOAEL: ♂♀ = 5000 ppm ♂ = 1484, ♀ = 1912 mg/kg bw/d	no effects on mortality (1♀ at 300 ppm died unrelated to treatment), clinical signs of toxicity, food intake, hematology or gross pathology 5000 ppm: ♂♀—↓ bw and bwg; centrilobular hepatocyte hypertrophy; myocardial vacuolation ♀—↑ total bilirubin
90-day dietary—rat	**Reg. No. 191 819** N32, 94.9%; rat, Wistar Chbb:THOM (SPF), 10/sex/group 0, 300, 3000, 5000 ppm (♂ = 0, 22, 223, 383; ♀ = 0, 26, 257, 440 mg/kg bw/d)	NOAEL: ♂♀ = 300 ppm (♂ = 22, ♀ = 26 mg/kg bw/d) LOAEL: ♂♀ = 3000 ppm (♂ = 223; ♀ = 257 mg/kg bw/d)	no deaths; no effects on clinical signs, ophthalmoscopy hematology, urinalysis, organ wts, or gross pathology 5000: ♂♀—↓ bw and bwg, food intake; ↑ creatinine and bilirubin; renal hyaline droplet degeneration ♂—centrilobular hepatocyte hypertrophy (2) 3000: ♂♀—↑ creatinine, bilirubin ♂—↓ bw and bwg, food intake
	Reg. No. 275 522, 00448-1, 91.3%; rat, Wistar; 10/sex/group 0, 300, 3000 and 5000 ppm (♂ = 0, 19, 196, 322; ♀ = 0, 23, 228, 388 mg/kg bw/d)	NOAEL: ♂+♀ = 5000 ppm ♂ = 322, ♀ = 388 mg/kg bw/d	no mortality; no effects on food intake, bw, bwg, ophthalmoscopy, hematology, clinical chemistry, urinalysis, organ wts, gross or histopathology 5000 ppm: ♂—bw and bwg consistently lower than control males, but not statistically significant

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
90-day dietary—dog	**Reg. No. 191 819** N41, 93%; 0, 400, 2000, 10 000 ppm (♂ = 0, 12.9, 63.3, 325 ♀ = 0, 14.3, 68, 358 mg/kg bw/d) dog, beagle, 6/sex/group	NOAEL ♂+♀ = 2000 ppm ♂ = 63.3, ♀ = 68 mg/kg bw/d LOAEL ♂ + ♀ = 10000 ppm ♂ = 325, ♀ = 358 mg/kg bw/d based on numerous effects on hematology, clinical chemistry, gross and histopathology	no deaths; no effects on clinical signs, ophthalmoscopy urinalysis 10 000 ppm: ♂♀—↓ food intake, bw, bwg (1♂, 2♀); RBC, Hb, Hct ↑ WBC (lymphocytes), platelets; AP, ALT, triglycerides, cholesterol, abs and rel wts of liver, thyroid (marginal and/or within normal range); enlarged liver; enlarged kidneys (2/sex), thyroid discoloration (2♂, 5♀); liver—hypertrophy and cholestasis; gallbladder—concrement; spleen hemosiderosis; sternum marrow hyperplasia urinalysis (↓ pH; ↑ SG, d85) ♂—urinalysis (↓ leucocytes; dark yellow, cloudy, 2♂); ↓ abs and rel testis wt; testis reduced size; lungs focal emphysema (3); testes giant cells and atrophy; epididymides atrophy; thyroid distended follicules ♀—↑ abs and rel kidney wt; spleen discoloration, extramedullary hematopoiesis and congestion (2) 2000 ppm: ♂—↑ abs liver wt, rel liver wt (marginal)
1-year dietary—dog	**Reg. No. 191 819** N41, 93%; 0, 100, 400 or 2000 ppm (♂ = 0, 3.0, 11.5, 56.0 ♀ = 0, 3.1, 12.5, 60.6 mg/kg bw/d) dog, beagle, 4/sex/dose	NOAEL: 400 ppm (♂ = 11.5, ♀ = 12.5 mg/kg bw/d LOAEL: 2,000 ppm (♂ = 56.0, ♀ = 60.6 mg/kg bw/d)	no mortality; no effects on clinical signs, bw, bwg, food intake, food efficiency, ophthalmoscopy, hematology, clinical chemistry or urinalysis 2000 ppm: ♂♀—diffuse hyperplasia of transitional epithelium in urinary bladder ♂—↓ epididymides wt, reduced activity of tubular epithelium of epididymides, reduced activity of epithelium of prostate; a few small transitional cell papillomas in urinary bladder (1♂)
	Reg. No. 191 819 N41, 93%; 0, 8000 ppm (♂ = 0, 248, ♀ = 0, 265 mg/kg bw/d) dog, beagle, 6/sex/dose	NOAEL: not determined LOAEL: 8 000 ppm (♂ = 248, ♀ = 265 mg/kg bw/d)	no mortality; no effects on clinical signs, bw, bwg, food intake, food efficiency, ophthalmoscopy or urinalysis 8000 ppm: ♂♀—↓ RBC, Hct, Hb, glucose, ↑ reticulocyte, platelets, total protein, globulin, ALAT, AP, bilirubin, cholesterol and triglyceride tissue pathology—spleen (hemosiderin deposition), bone marrow (femur and sternum) hyperplasia, liver (↑ wt, centrilobular hepatocellular hypertrophy, cholestasis), thyroid (↑ wt, distended follicles), urinary bladder (foci, discolouration, diffuse hyperplasia of transitional epithelium) ♂—↑ ASAT tissue pathology—gall bladder concrement, testes and epididymides (↓ wt, loss of spermatids/sperm, degeneration/atrophy of germinal epithelium, giant cells, ↓ tubular diameters and/or inactivated epithelium in epididymides, urinary bladder (focal hemorrhage), thyroid (C-cell hyperplasia)
4-week dermal—rat	**Reg. No. 191 819**, N41, 92.9%, in 0.1% aqueous CMC rat, Wistar; 5/sex/group 0, 50, 200, 1000 mg/kg bw/d, 6 h/d, 7 d/wk	systemic and dermal NOAEL ♂ + ♀ >1000 mg/kg bw/d	no mortality, no treatment-related clinical signs, local reaction, food intake, bw, hematology, clinical chemistry, hematology, organ weight, gross and histopathology

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
CHRONIC TOXICITY/ONCOGENICITY—Tepraloxydim technical (code name Reg. No. 191 819)			
18-month dietary—oncogenicity mouse	**Reg. No. 191 819** N41, 95.5%; mouse, C57BL/6N Crl BR; 50/sex/group 0, 200, 1800, 5000 ppm (♂ = 0, 37, 332, 1035; ♀ = 0, 52, 490, 1456 mg/kg bw/d)	NOAEL ♂ = 200 ppm (= 37 mg/kg bw/d) ♀ = not established LOAEL ♂ = 1800 ppm (= 332 mg/kg bw/d) ♀ = 200 ppm (= 52 mg/kg bw/d) based on bw and bwg **liver tumours in ♀ at exceedingly high dose of 1456 mg/kg bw/d; findings not relevant for carcinogenicity risk assessment for humans**	no treatment-related effects on mortality, clinical signs, differential blood counts, gross pathology mortality: ♂ = 7, 4, 4, 4; ♀ = 5, 9, 5, 4 5000 ppm: ♀—higher palpable masses in abdominal regions (28 versus 17 of control); ↑ liver adenoma and carcinoma (6 vs. 0 in control) ≥1800 ppm: ♂ + ♀—↓ bw (high-dose ♂♀ = 73 and 75% of control values at 1 yr; 70 and 77% of control values at study end); bwg (high-dose ♂♀ = 38 and 46% of control values at 1 yr; 30 and 50% of control values at study end) food intake and food efficiency highly variable liver histopathology (↓ weight, ↑ masses, foci of cellular alteration, cellular hypertrophy) reduced secretary activities of the seminal vesicles and preputial glands, uterine sclerosis and/or decreased ovarian activities 200 ppm: ♀—↓ bw, bwg
2-year dietary—rat	**Reg. No. 191 819**, N41, >95%; 0, 100, 600, 3000 (♂), 4000 (♀) ppm (♂ = 0, 5, 29, 154; ♀ = 0, 6, 38, 273 mg/kg bw/d) rat, Wistar, 20/sex/group	NOAEL ♂ + ♀ = 600 ppm ♂ = 29, ♀ = 38 mg/kg bw/d LOAEL ♂ = 3000 ppm, or 154 mg/kg bw/d ♀ = 4000 ppm, or 273 mg/kg bw/d **liver tumours in ♂**	no treatment-related effects on mortality, clinical signs, ophthalmoscopy, hematology, urinalysis, gross pathology mortality: ♂ = 7, 7, 3, 5; ♀ = 5, 5, 7, 5 3000/4000 ppm: ♂+♀—↓ food intake, bw; bwg, food efficiency; ↑ creatinine, protein, albumin, cholesterol, bilirubin (♀) liver histopathology (eosinophilic foci, cellular polymorphism; ♂—↑ liver adenoma and carcinoma (7 vs. 4 in control)
2-year dietary—oncogenicity rat	**Reg. No. 191 819**, N41, >95%; 0, 100, 600, 3000 (♂), 4000 (♀) ppm (♂ = 0, 5, 30, 155; ♀ = 0, 6, 38, 273 mg/kg bw/d) rat, Wistar, 50/sex/group	NOAEL ♂ = 100 ppm 5 mg/kg bw/d ♀ = 600 ppm 38 mg/kg bw/d LOAEL ♂ = 600 ppm, or 30 mg/kg bw/d ♀ = 4000 ppm, or 273 mg/kg bw/d **liver tumours in ♀**	no treatment-related effects on mortality, clinical signs, hematology, gross pathology mortality: ♂ = 15, 17, 15, 15; ♀ = 11, 14, 13, 10 3000/4000 ppm: ♂♀—↓ food intake, bw; bwg, food efficiency; liver histopathology (eosinophilic foci, cellular polymorphism, hepatocyte hypertrophy, fatty infiltration) ♀—↑ liver adenoma and carcinoma (7 vs. 1 in control) 600 ppm: ♂—↓ bwg, food efficiency early part of study; liver histopathology (eosinophilic foci) high incidence of adrenal tumours in control and test ♂ when compared to historical controls
Combined rat liver tumour data from both studies		**Insufficient evidence of induction of tumours in both sexes**	**incidence of liver tumours:** N = 70/group ♂: 0 / 100 / 600 / 3000 — ♀: 0 / 100 / 600 / 3000 adenoma: 4 3 6 5 — 4 1 3 6 carcinoma: 5 4 **9** **10** — 0 0 0 **3** combined: 9 7 **15** **15** — 4 1 3 **9** incidence of liver tumours was considered to be within historical control values and unrelated to the test article

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
MECHANISTIC STUDIES ASSESSING ONCOGENICITY—Tepraloxydim technical (code name Reg. No. 191 819)			
Hepatic enzyme induction—rat **non-guideline study**	**Reg. No. 191 819**, N41, 91.6%, rat, Wistar, 8/sex/group 0, 3000 (♂ 293 mg/kg bw/d), or 4000 ppm (♀ 416 mg/kg bw/d) for 1, or 3 wk	assessment of cyanide-insensitive palmitoyl-CoA-oxidation and protein in liver homogenate; glutathione concentration, cytochrome P450, ethoxyresorufin-O-deethylase (EROD), pentoxyresorufin-O-depentylase (PROD) and nitrophenol-hydroxylase in S-9 fraction; light and ultrastructural changes in liver sections	no clinical signs, no effects on liver weight, histo- and ultrastructural morphology of liver, glutathione, palmitoyl-CoA-oxidation, cytochrome P450 values of enzyme activities highly variable **no definitive conclusions** on hepatic enzyme induction by Reg. No. 191 819 supplementary information only
Foci-initiating activity—oral, rat, ♀ **non-guideline study**	**Reg. No. 191 819**, N41, 91.6%; in 0.5% CMC rat, Wistar, ♀, 30/group 0, 2000 mg/kg bw, positive control with foci-initiator NNM at 25 mg/kg bw	partial hepatectomy 14 d prior to treatment: 1. test article at 0 or 2000 mg/kg bw by oral gavage; foci-initiator NNM at 25 mg/kg bw 2. 2 wk after treatment 1, 15/group received basal diet; 15/group received diet with foci-promoter PB for 6 wk	no clinical signs; lower absolute and relative liver wt of rats exposed to a single oral dose of the foci-initiator NNM and test article without subsequent exposure to the promoter PB liver histopathology: NNM-treated groups: ↑ altered foci PB-treated groups: ↑ hepatocyte hypertrophy liver immunohistochemistry (foci of glutathione S-transferase activity): NNM and NNM+PB groups: ↑ negative control and test article groups: similar Reg. No. 191 819 not a foci-initiator
Initiation/promotion of hepatocarcino-genesis—dietary—rat, ♀ **non-guideline study**	**Reg. No. 191 819**, N41, 91.6%; rat, Wistar; ♀, 15/sex/group 0, 100, 400, 2000), or 4000 ppm (0, 9, 37, 187, 380 mg/kg bw/d); positive control dietary phenobarbital at 500 ppm (46 mg/kg bw/d) for 6 wk (wk 3–8)	rats were pretreated with IP injection of diethylnitrosamine (DEN) at 200 mg/kg bw (wk 1–2); partial hepatectomy on wk 3	no clinical signs, effects on food intake, liver weight or liver histopathology 4000: ↓ bw ≥2000: ↑ number and percent area of GST-P positive liver foci positive control: ↑ number and percent area of GST-P positive liver foci
DNA synthesis activity (S-phase response) in hepatocytes rat **non-guideline study**	**Reg. No. 191 819**, N41, 91.6%; rat, Wistar, 5/sex/group 0, 100, 600, 3000) (♂), or 4000 (♀) ppm (♂ = 0, 6.2, 36.6, 183; ♀ = 0, 7.2, 44.4, 297.2 mg/kg bw/d) for 1, 6, or 13 weeks; some groups with recovery periods		no mortality or clinical signs of toxicity, no effects on liver gross or histopathology 3000/4000 ppm: ♂♀—↓ fd, bw; ↑ DNA synthesis after 1, 6, 13 wk without recovery periods 600 ppm: ♂♀—↑ DNA synthesis after 1, 6, 13 wk without recovery periods
Analysis of bilirubin and creatinine by standard colorimetrical method and enzymatic methods dietary rat **non-guideline study**	**Reg. No. 191 819**, 92.6%; rat, Wistar; 5/sex/group 0, 10 000 ppm (♂ = 0, 899; ♀ = 0, 870 mg/kg bw/d) for 2 weeks		no mortality, no clinical signs of toxicity 10 000 ppm: ♂—↓ fd, bw; serum bilirubin and creatinine levels: standard colorimetric method: ♂♀—↑ in test rats enzymatic method: similar between test and control rats

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
GENOTOXICITY—Tepraloxydim technical (code name Reg. No. 191 819)			
Salmonella/Ames test (in vitro)	**Reg. No. 191 819**, N32, 94.95%; in dimethylsulfoxide (DMSO); *S. typhimurium* TA98, TA100, TA1535, TA1537 at 0, 4 (assay 2), 20, 100, 500, 2500, or 5000 (assay 1) µg/plate; ±S9	not mutagenic	cytotoxicity: ≥2500 µ/plate precipitation: no precipitation revertant colonies: similar among solvent controls and test groups; significant increase in positive control groups not mutagenic
Mammalian gene mutation (in vitro)	**Reg. No. 191 819**, N32, 94.95%, in DMSO, CH ovary K1 cells ±S9: 0 (untreated), 0 (solvent), 187.5, 375, 750, 1500, or 3000 µg/mL	not mutagenic	precipitation: no precipitation cytotoxicity: not cytotoxic mutation frequency: /10^6 cells Controls / Test groups / +ve controls -S9: 0.4–2.6 / 0–9.2 / **203, 249** +S9: 0–8.1 / 0–9.0 / **158, 344**
Mammalian chromosomal aberration (in vitro)	**Reg. No. 191 819**, N32, 94.95%; in DMSO; CHO cells assay 1: µg/mL ±S9: 0 (untreated), 0 (vehicle), 62.5, 125, 250, 500, 1000; 21 h assessment assay 2: µg/mL ±S9: 0, 0, 250, 500, 1000; 21 and 45 h assessment	positive controls: -S9: methylmethane sulfonate +S9: cyclophosphamide not clastogenic	p precipitation: slight at 1000 µg/mL cytotoxicity: no evidence aberrant cells/100 cells: with gaps Untreated / Solvent / Test substance / Positive assay 1: -S9: 2.5 / 8.0 / 6.0–9.0 / **39.0** +S9: 4.5 / 8.5 / 3.5–7.0 / **68.0** assay 2: -S9 21-h: 7.5 / 7.0 / 1.0–6.5 / **35.0** 45-h: 3.0 / 5.0 / 4.0–6.5 +S9 21-h: 5.0 / 4.5 / 4.0–8.0 / **54.0** 45-h: 2.0 / 4.0 / 2.0–6.5
Micronucleus assay (in vivo) in mouse	**Reg. No. 191 819**, N41, 93%, in DMSO; intraperitoneally at 0, 125, 250, 500 mg/kg bw mouse, NMRI, 5/sex/gp/sacrifice interval (24h; additional sacrifice at 48 h for vehicle and high-dose gps); 1000 PCEs from marrow of tibiae/animal assessed	positive controls: 1. cyclophosphamide, 20 mg/kg bw; intraperitoneally 2. vincristine, 0.15 mg/kg bw; intraperitoneally	toxicity: vehicle gp—nil positive controls—nil test gps—minimal irregular respiration, abdominal position and/or apathy micronucleus analysis: micronucleated PCE/1000 PCE vehicle control = 1.4–1.6 test groups =1.7–2.4 cyclophosphamide = **20.4** vincristine = **131** not clastogenic
UDS in rat primary hepatocyte (in vitro)	**Reg. No. 191 819**, N41, 92.9%, in DMSO, assay 1: 0 (untreated), 0 (vehicle), 0.1, 0.5, 1.0, 5.0, 10, 50, 100, or 500 µg/mL assay 2: 0, 0. 5, 10, 50, or 100 µg/mL 18–20 h exposure; 100 nuclei/level assessed	positive control : 2-acetyl-aminofluorene (2-AAF), 4.5 µg/mL	cytotoxicity: ≥100 µg/mL UDS: -ve controls / Test / Positive net nuclear grain: -(4.93–6.16) / -(4.06–6.77) / **2.19–14** cells w nng ≥0, % 2 / 2–7 / **62, 92** cells w nng ≥5, % 0 / 0–1 / **27, 80** negative
GENOTOXICITY—5-OH-tepraloxydim (code name Reg. No. 275 522), a major plant metabolite of tepraloxydim			
Salmonella/Ames test (in vitro)	**Reg. No. 275 522**, 00448-1; 89.6%, in DMSO; *S. typhimurium* TA98, TA100, TA1535, TA1537; ±S9: 0, 20, 100, 500, 2500, 5000 µg/plate	not mutagenic	cytotoxicity: ≥2500 µg/plate precipitation: no precipitation revertant colonies: similar among solvent controls and test groups; significant increase in positive controls not mutagenic

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Micronucleus assay (in vivo) in mouse	**Reg. No. 275 522,** 00448-1; 91.3%, in 0.5 aqueous CMC; intraperitoneally at 0, 375, 750, 1500 mg/kg bw mouse, NMRI, 5/sex/gp/sacrifice interval (24h; additional sacrifice at 48 h for vehicle and high-dose gps); 1000 PCEs from marrow of tibiae/animal assessed	positive controls: 1. cyclophosphamide, 20 mg/kg bw; intraperitoneally 2. vincristine, 0.15 mg/kg bw; intraperitoneally	toxicity: vehicle gp—nil positive controls—nil test gps—within 30–60 min, squatting posture, piloerection micronucleus analysis: micronucleated PCE/1000 PCE vehicle control = 1.6–2.7 test groups =1.7–2.6 cyclophosphamide = **11.4** vincristine = 35 not clastogenic
UDS in rat primary hepatocyte (in vivo / in vitro)	**Reg. No. 275 522,** 00448-1; 92.3%, rat, Wistar, ♂; 8/group 0, 1000, 2000 mg/kg bw	positive control : 2-AAF, 100 mg/kg bw	cell viability, all groups all time intervals: 73–88% UDS: -ve controls Test Positive net nuclear grain: -1.77, -3.63 -(1.96–3.77) **14, 23** negative
UDS in rat primary hepatocyte (in vitro)	**Reg. No. 275 522,** 00448-1; 91.3%, in DMSO; 2 assays 0 (untreated), 0 (vehicle), 37.5, 75, 150, 300, 600, 1200, 2400, or 3600 µg/mL 18–20 h exposure; 100 nuclei/level assessed	positive control : 2-acetyl-aminofluorene, 4.0 µg/mL	cytotoxicity: ≥2400 µg/mL UDS: -ve controls Test Positive net nuclear grain: -(3.99–6.55) -(2.75–5.23) **16, 26.5** cells w nng ≥0, % 0–9 **10–24** **93, 97** cells w nng ≥5, % 0 0–2 **90, 93** marginal
REPRODUCTION/DEVELOPMENTAL TOXICITY—Tepraloxydim technical (code name Reg. No. 191 819) and 5-OH-tepraloxydim (code name Reg. No. 275 522)			
2-generation reproductive toxicity—rat	**Reg. No. 191 819**, N41, 93%; 0, 100, 500, 2500 ppm (♂ = 0, 10.2, 50.9, 253.1 ♀ = 0, 11.2, 54.7, 273.8 mg/kg bw/d) rat, Wistar 25/sex/group	NOAEL parental/offspring = 500 ppm ♂ = 50.9, ♀ = 54.7 mg/kg bw/d reproductive > 2500 ppm ♂ = 253.1, ♀ = 273.8 mg/kg bw/d LOAEL parental/offspring = 2500 ppm ♂ = 253.1, ♀ = 273.8 mg/kg bw/d	litters: 23–25 parental toxicity: 2500 ppm: ↓ food, bw during premating, gestation and lactation periods of both generations; ↑ creatinine reproductive toxicity: nil offspring toxicity: 2500 ppm—↓ pup wt; delayed development (F_2 pups; eye opening, pinna unfolding and auditory canal opening)
Teratogenicity rat	**Reg. No. 191 819**, N41, 93%; 0, 40, 120, 360 mg/kg bw/d rat, Wistar 25/sex/group dosing gestation d 6–15 sacrifice gestation d 20	NOAEL, mg/kg bw/d maternal = 120 developmental = 40 teratogenicity = 120 LOAEL mg/kg bw/d maternal = 360 developmental = 120 teratogenicity = 360 **teratogenic** at 360 mg/kg bw/d **offspring toxicity at maternal non-toxic level**	dams with live fetuses: 23, 24, 23, 24 at 0, 40, 120, 360 mg/kg bw/d, respectively no mortality maternal toxicity: 360: ↓ bw and food intake developmental toxicity: 360: ↑ resorptions, skeletal retardations, hydroureter; ↓ gravid uterine wt, mean fetal wt 120: ↑ skeletal retardations, hydroureter; ↓ mean fetal wt teratogenicity: 360: 3/2 (fetuses/litters) with dilation of heart ventricle, 2/2 with filiform tail, absent caudal and sacral vertebrae

STUDY	TGAI, PURITY; SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/d	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
	Reg. No. 191 819, 92/268, 92.6%; 0, 10, 20, 40 mg/kg bw/d rat, Wistar 25/sex/group dosing gestation d 6–15 sacrifice gestation d 20	NOAEL = 40 mg/kg bw/d for maternal and developmental toxicity LOAEL > 40 mg/kg bw/d for maternal and developmental toxicity **not teratogenic**	dams with live fetuses: 23, 23, 23, 25 at 0, 10, 20, 40 mg/kg bw/d, respectively no effects on mortality, clinical signs, food intake, bw, gross histopathology, organ wt, reproductive parameters, offspring toxicity, developmental toxicity, teratogenicity 40 mg/kg bw/d: ↓(marginally) bwg during dosing period
	Reg. No. 275 522, 00448-1, 91.3%; 0, 20, 40, 120, 360 mg/kg bw/d rat, Wistar, 25/sex/group dosing gestation d 6–15 sacrifice gestation d 20	NOAEL, mg/kg bw/d maternal = 120 developmental = 360 LOAEL mg/kg bw/d maternal = 360 developmental >360 **not teratogenic**	dams with live fetuses: 24, 24, 24, 25, 23 at 0, 20, 40, 120, 360 mg/kg bw/d, respectively no mortality maternal toxicity: 360: ↓ bwg during gestation days 6–20 developmental toxicity: no effects teratogenicity: no findings
Teratogenicity—rabbit	**Reg. No. 191 819**, N41, 93%; 0, 20, 60, 180 mg/kg bw/d in 0.5% aqueous CMC; oral gavaged at gestation d 7–19; sacrifice d 29 rabbit, Himalayan (Chbb:HM) 15 inseminated ♀/group	NOAEL, mg/kg bw/d maternal = 60 developmental = 180 (HDT) LOAEL, mg/kg bw/d maternal = 180 **not teratogenic**	no treatment-related effects on mortality, clinical signs, gross pathology, gravid uterus weights, fetal body weights, sex ratios, placental weight, implantation, early or late resorption, fetal malformation or anomalies maternal toxicity: 180: ↓ food intake, bwg fetotoxicity: nil teratogenicity: no evidence
NEUROTOXICITY—Tepraloxydim technical (code name Reg. No. 191 819)			
Acute—rat	**Reg. No. 191 819**, N41, 93%; oral gavage at 0, 500, 1000, 2000 mg/kg bw in 1% aqueous CMC; rat, Wistar, 10/sex/group 14 d observation	NOAEL, mg/kg bw/d ♂ = 2000; ♀ = not defined LOAEL, mg/kg bw/d ♂ = not defined; ♀ = 500 **not neurotoxic**	no deaths, no effects on clinical signs, bw, functional observation battery, gross or histopathology of nervous tissues ≥ 1000 mg/kg bw: ♀—↓ motor activity initially in on d 0; possibly pharmacological in nature
90-day dietary rat	**Reg. No. 191 819**, N41, 92.9%; 0, 400, 1500, 6000 ppm (♂ = 0, 28, 103, 428 mg/kg bw/d ♀ = 0, 33, 124, 513 mg/kg bw/d) rat, Wistar; 10/sex/group	NOAEL = 1500 ppm ♂ = 103, ♀ = 124 mg/kg bw/d LOAEL = 6000 ppm ♂ = 428, ♀ = 513 mg/kg bw/d **not neurotoxic**	no deaths, no effects on clinical signs, functional observation battery, gross or histopathology of nervous tissues 6000 ppm: ♂♀—↓ food intake, bw, bwg; ↑ motor activity
Recommended ARfD: 1. General population: not required because of the relatively low acute toxicity 2. Women of child-bearing age (13–50 years of age): because of the teratogenic concerns observed in the rat study, an ARfD of 0.13 mg/kg bw is determined based on the developmental NOAEL of 40 mg/kg bw/d, a standard UF of 100 and a safety factor of ×3 for offspring toxicity at a maternally non-toxic dose.			
Recommended ADI: 0.02 mg/kg bw/d based on the NOAEL of 5 mg/kg bw/d established in male rats in the 2-year oncogenicity study, an UF/SF of 100, ×3 factor due to higher sensitivity of young.			

Appendix II Residues

Table 1 Integrated food residue chemistry summary

DIRECTIONS FOR USE OF PESTICIDE ON X CROPS						
Crop	**Formulation/ type**	**Timing**	**Rate g a.i./ha**	**#/season**	**Maximum rate g a.i./ha**	**PHI (days)**
Flax	EC	Ground app./ Emergence to 50 cm	33–50	1	50	60
Lentils	EC	Ground app./ Emergence to 12 leaf (50 cm)	33–50	1	50	60
Dry peas	EC	Ground app./ Emergence to 9 leaf (50 cm)	33–50	1	50	60
Label restrictions -Grazing on peas may be allowed provided the 60-day PHI is followed. -Grazing on lentils and flax (or cut for hay) is not supported. -A 40-day PBI is required.						

PHYSICOCHEMICAL PROPERTIES	
Water solubility at 25°C (mg/L)	430 (pH 6.5); 7250 (pH 9.0)
Solvent solubility (Temperature not specified) (g/L)	70 g/100 mL in acetone; 33 g/100 mL in methanol; 16 g/100 mL in 2-propanol; 69 g/100 mL in ethyl acetate; 77 g/100 mL in acetonitrile; 119 g/100 mL in dichloromethane; 82 g/100 mL in toluene; 1.0 g/100 mL in n-heptane; 15 g/100 mL in 1-octanol; 8.0 g/100 mL in olive oil
Octanol–water partition coefficient (Log K_{ow}) at 25°C	1.5 (pure water); 2.44 (pH 4); 0.20 (pH 7); -1.15 (pH 9)
Dissociation constant (pK_a) at 25°C	pK_a = 4.58
Vapour pressure at 25°C	2.7×10^{-7} hPa
Relative density (g/cm^3)	1.284 g/cm^3
Melting point °C	72.5–74.4
UV–Visible absorption spectrum	λ (nm) / ϵ (l×mol^{-1}×cm^{-1}) 204 / 9.5×10^3 225 / 4.6×10^3 258 / 1.1×10^4 290 / 6.8×10^3 300 / 3.1×10^3 Not expected to absorb UV at λ >350 nm.

ANALYTICAL METHODOLOGY				
Parameters	**Plant matrices**			
Method ID	**587**	**D9701/1**	**D9704/1**	**620-DD-F**
Type	Data-gathering	Data-gathering	Data-gathering and enforcement	Data-gathering
Analytes	DMP and OH-DMP	DMP and OH-DMP	GP and OH-GP	DD
Instrumentation	GC/MS	GC/MS	LC/MS/MS	HPLC/UV and LC/MS
LOQ	0.10 ppm	0.10 ppm	0.10 ppm	0.05 ppm
Interlaboratory validation	No interlaboratory validation study was provided.	Interlaboratory validation study showed marginal recoveries, but standard deviations were low so correction factors could be applied	Interlaboratory validation study was acceptable	No interlaboratory validation study was provided.
Extraction/clean up	Residues are extracted with aqueous MeOH. After partitioning with isopropanol and evaporation of MeOH, $Ca(OH)_2$ is added to precipitate impurities. Following oxidation and methylation, NH_2 and C_{18} SepPak columns are used for clean-up.	Residues are extracted with aqueous MeOH. After partitioning with isopropanol and evaporation of MeOH, $Ca(OH)_2$ is added to precipitate impurities. Following oxidation and methylation, a Florisil column is used for clean-up.	Residues are extracted with aqueous MeOH. After partitioning with isopropanol and evaporation of MeOH, $Ca(OH)_2$ is added to precipitate impurities. Following oxidation, a C_{18} column is used for clean-up.	Residues are extracted with aqueous MeOH. After partitioning with isopropanol and evaporation of MeOH, $Ca(OH)_2$ is added to precipitate impurities. A Sep Pak column is used for clean-up.
Radiovalidation	Adequately radiovalidated	None	None	Adequately radiovalidated
Multiresidue method	Protocols A through F are not suitable for analysis of tepraloxydim residues.			

Parameters	Animal matrices		
Method ID	389/0	780	975/1
Type	Data-gathering and enforcement	Data-gathering	Data-gathering
Analytes	DMP, OH-DMP and DML	DMP, OH-DMP and DML	DMP, OH-DMP and DML
Instrumentation	GC/MS	GC/MS	GC/MS
LOQ	0.03 ppm for milk and cream; 0.15 ppm for tissues	0.15 ppm	0.15 ppm
ILV	ILV study was acceptable	None	None
Extraction/ clean-up	Residues are extracted from milk and cream using ACN:hexane, and from tissues using aqueous MeOH. $Ca(OH)_2$ is used to precipitate impurities. Silica gel and SPE phenyl columns are used for final clean-up.	Residues are extracted from tissues using aqueous MeOH. $Ca(OH)_2$ is used to precipitate impurities. Silica and C_{18} columns are used for final clean-up.	Residues are extracted from tissues using aqueous MeOH. $Ca(OH)_2$ is used to precipitate impurities. Silica gel and SPE phenyl columns are used for final clean-up.
Radiovalidation	Adequately radiovalidated	Adequately radiovalidated	Adequately radiovalidated
Multiresidue method	Protocols A through F not suitable for analysis of tepraloxydim residues.		

NATURE OF THE RESIDUE IN PLANTS—SOYBEANS		
Radiolabel position	[cyclohexene-4(6)-^{14}C]tepraloxydim	[pyran-4-^{14}C]tepraloxydim
Test site	Indoor test pots	Indoor test pots
Treatment	Postemergent application, 51 d after seeding	Postemergent application, 51 d after seeding
Rates	100 and 300 g a.i./ha	100 and 300 g a.i./ha
Seasonal rates	100 and 300 g a.i./ha	100 and 300 g a.i./ha
PHI	60 d	60 d
Tepraloxydim is taken up by soybeans, translocated throughout the plant and is extensively metabolized.		

Metabolites identified										
[cyclohexene-4(6)-^{14}C]tepraloxydim										
Metabolite	Forage 30 DAT (TRR = 3.54 ppm)		Seed 60 DAT (TRR = 1.62 ppm)		Leaves 60 DAT (TRR = 35.19 ppm)		Stalk 60 DAT (TRR = 0.[illegible] ppm)		Pods 60 DAT (TRR = 1.57 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Tepraloxydim	25.83	0.915	7.85	0.125	14.05	4.946	9.23	0.044	3.49	0.05
5-OH-DP	ND	—	16	0.258	ND	—	ND	—	ND	—
DD	3.91	0.139	5.88	0.094	1.03	0.363	2.14	0.01	4.41	0.07
DD-2	0.69	0.02	0.72	0.011	0.89	0.314	1.33	0.01	0.43	0
DP-1	1.56	0.05	0.91	0.015	3.2	1.121	0.8	0	1.47	0.02
DP-2	3.07	0.108	0.52	0.01	2.53	0.887	ND	—	1.06	0.02
DP-6	ND	—	6.05	0.097	4.4	1.549	1.49	0.01	ND	—
15 (tetrahydro-DP)	0.7	0.02	0.09	0	0.57	0.199	ND	—	ND	

NATURE OF THE RESIDUE IN PLANTS—CANOLA	
Radiolabel position	[cyclohexene-4(6)-^{14}C]tepraloxydim
Test site	Outdoors in plastic pots
Treatment	45 days after seeding at the 6- to 8-leaf stage
Rate	100 or 300 g a.i./ha
Seasonal rate	100 or 300 g a.i./ha
PHI	61/67 d
Tepraloxydim is taken up by canola, translocated throughout the plant and is extensively metabolized.	

Metabolites identified				
[cyclohexene-4(6)-^{14}C]tepraloxydim				
Metabolite	Seed		Straw	
	% TRR	ppm	% TRR	ppm
Tepraloxydim	—	—	2.1	0.035
5-OH-DP	38	0.42	1.6	0.027
6-OH-DP-2	5.8	0.064	4.2	0.068
5-OH-DP-1	7.8	0.086	6.7	0.109
DD-2	—	—		
DD	—	—	3.8	0.062
DP-2	—	—	3.1	0.05
DP-1	—	—	1.8	0.029

[cyclohexene-4(6)-^{14}C]tepraloxydim				
Metabolite	Seed		Straw	
	% TRR	ppm	% TRR	ppm
DD-4	—	—	3.3	0.052
DD-1	—	—	4.2	0.069
GP	—	—	10.2	0.166
DD-6	—	—	2.2	0.036

NATURE OF THE RESIDUE IN PLANTS—SUGAR BEETS
Metabolism study of [cyclohexene-4(6)-^{14}C]tepraloxydim in/on sugar beets is not valid since 24.9–49.2% of the TRR was not identified/characterized.

CONFINED ROTATIONAL CROP STUDY—Radish, chard, sorghum, wheat		
Radiolabel position	[cyclohexene-4(6)-^{14}C]tepraloxydim	[pyran-4-^{14}C]tepraloxydim
Test site	Confined plots	Confined plots
Formulation used for trial	toluene	toluene
Application rate and timing	112 g a.i./ha	112 g a.i./ha
Metabolites identified		
Radiolabel position	[cyclohexene-4(6)-^{14}C]tepraloxydim	[pyran-4-^{14}C]tepraloxydim
Radish roots PBI 40 d	DP-2, <0.001 ppm (<1.1% TRR)	0.001 ppm (1.7% TRR)

NATURE OF THE RESIDUE IN LAYING HEN—Tepraloxydim			
Species	Dose level	Length of dosing (d)	Sacrifice (h)
Hen	0.7 (low dose) and 15.4 (high dose)	8 (low dose) and 5 (high dose)	23 (low dose) and 3 (high dose) after last dose
82.4–93.7% TRR was eliminated in excreta and cage wash; radioactivity recovered from eggs ranged from 0.59–0.74% TRR; radioactivity recovered from all other tissues ranged from 0.43–6.60% TRR.			

Metabolites identified												
Radiolabel position	[cyclohexene-4(6)-^{14}C]tepraloxydim											
Metabolite	Egg whites (4.64 ppm)		Egg yolks (0.910 ppm)		Liver (14.9 ppm)		Muscle (3.93 ppm)		Fat (3.02 ppm)		Skin (4.95 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Tepraloxydim	23.4	1.09	6.7	0.06	20.6	3.07	14.8	0.58	45.6	1.37	39.2	1.9
2-OH-P-DP	10.3	0.48	—	—	1.3	0.19	12	0.47	—	—	3.9	0.2
2-OH-P-DP-2	0.7	0.03	—	—	1	0.15	4.9	0.19	—	—	1.3	0
DD	—	—	—	—	2.6	0.39	—	—	—	—	—	—
DL	4.8	0.22	0.8	0.01	1.8	0.26	1.5	0.1	—	—	5.7	0.3
DL-1	1.7	0.08	—	—	—	—	—	—	—	—	—	—
DL-2	1	0.05	—	—	2.2	0.32	0.5	0	—	—	0.6	0
DL-6	6.1	0.28	3.8	0.03	7.2	1.08	2.4	0.1	—	—	—	—
DP-1	3.2	0.15	—	—	5.9	0.89	3.2	0.13	3	0.1	1.7	0
DP-2	7.7	0.36	22.1	0.2	4.6	0.68	9	0.35	15	0.45	17.6	0.9
DP-4	2.1	0.1	—	—	—	—	1.7	0.1	1.9	0.1	—	—
DP-6	8.9	0.41	6.9	0.06	7	1.05	14.6	0.57	9.1	0.28	17.4	0.9
NH2-DP	2	0.09	—	—	—	—	—	—	—	—	—	—

NATURE OF THE RESIDUE IN LAYING HEN—5-OH-DP			
Species	Dose level (mg a.i./kg bw/d)	Length of dosing (d)	Sacrifice (h)
Hen	0.68 (low dose) and 17.2 (high dose)	8 (low dose) and 5 (high dose)	23 (low dose) and 3 (high dose) after last dose
71.8–95.7% TRR was eliminated in excreta and cage wash; 0.87–0.80% TRR recovered from eggs; 0.13–1.0% TRR recovered from other tissues.			

Metabolites identified												
Radiolabel Position	[cyclohexene-4(6)-^{14}C]5-OH-DP											
Metabolite	Egg whites (7.83 ppm)		Egg yolks (1.05 ppm)		Liver (7.69 ppm)		Muscle (3.93 ppm)		Fat (0.642 ppm)		Skin (3.95 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
5-OH-DP	76.7	6.01	58.7	0.62	44.7	3.44	64.4	2.53	72.2	0.46	65	2.5
5-OH-DP-1	4.8	0.38	3.7	0	4.3	0.33	7	0.28	4.1	0	6.1	0.2
5-OH-DP-2	4.5	0.35	10.3	0.11	6.5	0.5	9	0.36	4.6	0	11	0.4
5-OH-DP-4	0.6	0.05	—	—	—	—	—	—	1.4	0	—	—
5-OH-DP-6	11.5	0.9	10.7	0.11	11.2	0.86	6.9	0.27	5.8	0	7.1	0.3

NATURE OF THE RESIDUE IN RUMINANT—Tepraloxydim			
Species	Dose level (mg a.i./kg bw/day)	Length of dosing (d)	Sacrifice (h)
Goat	0.33 (low dose) and 7.43 (high dose)	5 (low dose) and 7 (high dose)	23 (low dose) and 3.8 (high dose)
76.5–90.6% TRR was eliminated in excreta and urine; 0.14–0.25% TRR was recovered from milk; 5.18–14.43% TRR was recovered from other tissues.			

Metabolites identified										
Radiolabel position	[cyclohexene-4(6)-^{14}C]tepraloxydim									
Metabolite	Milk (0.569 ppm)		Liver (11.29 ppm)		Kidney (13.05 ppm)		Muscle (2.06 ppm)		Fat (1.25 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Tepraloxydim	30.9	0.176	9.7	1.091	30.7	4.009	61	1.252	71.8	0.817
DL	19.5	0.11	4.9	0.547	7.4	0.968	5.3	0.109	—	—
2-OH-P-DP	3.9	0.022	0.7	0.086	5.3	0.691	7.3	0.15	—	—
DL-1	5.7	0.032	—	—	2.9	0.379	—	—	—	—
DL-2	—	—	1.1	0.121	—	—	—	—	—	—
DP-1	—	—	6.7	0.752	2.7	0.352	1.9	0.04	—	—
DP-2	—	—	2.4	0.275	—	—	—	—	—	—
620M015	1	0.01	—	—	—	—	—	—	—	—
N15	—	—	16.5	1.861	1.6	0.204	—	—	—	—
DD	—	—	0.3	0.037	1.2	0.162	—	—	—	—
DP-6	—	—	0.3	0.03	—	—	—	—	—	—
Glucuronic acid conj. tepraloxydim	—	–	–	–	10	1.308	—	—	—	—
620M043	—	—	0.1	0.016	—	—	—	—	—	—

Radiolabel Position	[pyran-4-^{14}C]tepraloxydim									
Metabolite	Milk (0.280 ppm)		Liver (17.81 ppm)		Kidney (11.33 ppm)		Muscle (2.93 ppm)		Fat (2.70 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Tepraloxydim	11.8	0.034	16.7	2.99	34.7	3.93	44	1.29	53.5	1.44
DL	9.4	0.026	—	—	4.9	0.55	—	—	—	—
2-OH-P-DP	12.3	0.034	—	—	18.4	2.08	13.5	0.4	5.7	0.15
DP-1	—	—	17.6	3.13	—	—	—	—	—	—
N15	—	—	8.9	1.59	—	—	—	—	—	—
Tepraloxydim-glucuronic acid conjugate	—	—	—	—	11.1	1.25	—	—	—	—

NATURE OF THE RESIDUE IN RUMINANT—5-OH-DP			
Species	Dose level (mg a.i./kg bw/day)	Length of dosing (d)	Sacrifice (h)
Goat	0.26 (low dose) and 8.04 (high dose)	6 (low dose) and 8 (high dose)	23 (low dose) and 3 (high dose)
83.1–90.2% TRR was eliminated in excreta and urine. 0.09–0.1% TRR was recovered from milk. 2.20–7.09% TRR was recovered from other tissues.			

Metabolites identified						
Radiolabel position	[cyclohexene-4(6)-^{14}C]5-OH-DP					
Metabolite	Milk (0.008 ppm)		Kidney (0.041 ppm)		Liver (0.035 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
5-OH-DP	36	0.003	33.4	0.014	12.7	0.004
5-OH-DP-1	15.3	0.001	11.3	0.005	7.6	0.003
6-OH-DP-2	8.5	0.001	2.6	0.001	4.2	0.001
5-OH-M04	—	—	0.7	<0.001	1.3	<0.001
5-OH-M05	—	—	2	0.001	1	<0.001
5-OH-M10	21	0.002	2.3	0.001	2.9	0.001
5-OH-M11	5.1	<0.001	2.6	0.002	1	<0.001
5-OH-M18	—	—	—	—	3	0.001
5-OH-DP-6	—	—	—	—	trace	<0.001
5-OH-M28	—	—	6.2	0.003	2.7	0.001

CROP FIELD TRIALS—Lentils

12 individual field trials were carried out on lentils in Canada at 1× and 2× the maximum label rate (in zones 5, 7 and 14) between 1995 and 1996.

Commodity	Total rate kg a.i./ha	PHI (days)	Analyte	Residue levels (ppm)				
				n	Min.	Max.	HAFT	Mean
Lentil seed	0.1	60	Total*	16	<0.10	<0.10	<0.10	<0.10
Lentil seed	0.05	60–67	Total*	16	<0.10	<0.10	<0.10	<0.10
Lentil seed	0.1	60–67	Total*	16	<0.10	<0.10	<0.10	<0.10

*Total = Tepraloxydim and metabolites convertible to DMP + 5-OH-DP and metabolites convertible to OH-DMP

RESIDUE DECLINE

No residue decline data were submitted, as all residues were below the LOQ.

CROP FIELD TRIALS—Dry Peas

12 individual field trials were carried out on dry peas in Canada at 1× and 2× the maximum label rate (in zones 5, 7 and 14) between 1995 and 1996.

Commodity	Total rate kg a.i./ha	PHI (days)	Analyte	Residue levels (ppm)				
				n	Min.	Max.	HAFT	Mean
Dry pea forage	0.1	15–18	Total*	16	<0.10	0.148	0.126	0.107
Dry pea seed	0.1	59–60	Total*	16	<0.10	<0.10	<0.10	<0.10
Dry pea forage	0.05	17–21	Total*	12	<0.10	<0.10	<0.10	<0.10
Dry pea forage	0.1	17–21	Total*	12	<0.10	<0.10	<0.10	<0.10
Dry pea seed	0.05	60–61	Total*	16	<0.10	<0.10	<0.10	<0.10
Dry pea seed	0.1	60–61	Total*	16	<0.10	<0.10	<0.10	<0.10

*Total = Tepraloxydim and metabolites convertible to DMP + 5-OH-DP and metabolites convertible to OH-DMP

RESIDUE DECLINE

No residue decline data were submitted, as all residues in edible fraction were below the LOQ.

CROP FIELD TRIALS—Flax

12 individual field trials were carried out on flax in Canada at 1× and 2× the maximum label rate (in zones 5, 7 and 14) between 1995 and 1996.

Commodity	Total rate kg a.i./ha	PHI (days)	Analyte	Residue levels (ppm)				
				n	Min.	Max.	HAFT	Mean/Median
Flax seed	0.1	59–60	Total*	16	<0.10	0.12	0.11	0.1
Fax seed	0.05	59–60	Total*	16	<0.10	<0.10	<0.10	<0.10
Flax seed	0.1	59–60	Total*	16	<0.10	<0.10	<0.10	<0.10

*Total = Tepraloxydim and metabolites convertible to DMP + 5-OH-DP and metabolites convertible to OH-DMP

RESIDUE DECLINE

No residue decline data were submitted, as residues were at or below the LOQ.

MAXIMUM RESIDUE LIMITS

Lentils, dry peas and flax	0.10 ppm
Milk	0.03 ppm
Eggs	0.15 ppm
Meat and meat byproducts	0.15 ppm

FIELD ACCUMULATION IN ROTATIONAL CROPS

Not submitted or required.

PROCESSED FOOD AND FEED

Fraction	Mean residue levels (ppm)	Concentration factor
Canola meal	0.52–1.08	0.70–0.95
Canola crude oil	0.14–0.30	0.19–0.25
Canola refined oil	0.10–0.11	0.07–0.18

LIVESTOCK FEEDING

The estimated maximum theoretical dietary burden (MTDB) is 0.20 ppm for cattle and 0.05 ppm for poultry.

Tissues/matrices	Feeding level	Maximum residue levels (ppm)	Anticipated residues* (ppm)
Poultry eggs	5 ppm	0.20	<0.15
Poultry muscle	5 ppm	0.17	<0.15
Poultry liver	5 ppm	0.73	<0.15
Poultry fat	5 ppm	0.19	<0.15
Milk	50 ppm	0.06	<0.03
Cattle muscle	5 ppm	<0.151	<0.15
Cattle liver	5 ppm	<0.150	<0.15
Cattle kidney	5 ppm	<0.150	<0.15
Cattle fat	5 ppm	<0.150	<0.15
			*All below LOQ

Table 2 Food residue chemistry overview of metabolism studies and risk assessment

PLANT STUDIES	
ROC FOR ENFORCEMENT (Figure 2.3.3.1) **Primary Crops**	Tepraloxydim and metabolites convertible to GP + 5-OH-DP and metabolites convertible to OH-GP
Rotational Crops	Tepraloxydim and metabolites convertible to GP + 5-OH-DP and metabolites convertible to OH-GP
ROC FOR RISK ASSESSMENT (Figure 2.3.3.1)	
Primary Crops	Tepraloxydim and metabolites convertible to GP + 5-OH-DP and metabolites convertible to OH-GP
Rotational Crops	Tepraloxydim and metabolites convertible to GP + 5-OH-DP and metabolites convertible to OH-GP
METABOLIC PROFILE IN DIVERSE CROPS	Metabolism for legume vegetables (Crop Group 6) and oilseeds (Crop Group 12) understood but qualitatively and quantitatively different. Third crop study (sugar beets) not valid.
ANIMAL STUDIES	
ANIMALS	**Poultry and ruminant**
ROC FOR ENFORCEMENT (Figure 2.3.4.1)	Tepraloxydim and metabolites convertible to DMP + 5-OH-DP and metabolites convertible to OH-DMP + Metabolites convertible to DML
ROC FOR RISK ASSESSMENT (Figure 2.3.4.1)	Tepraloxydim and metabolites convertible to DMP + 5-OH-DP and metabolites convertible to OH-DMP + Metabolites convertible to DML
METABOLIC PROFILE IN ANIMALS	Similar
FAT SOLUBLE RESIDUE	Yes, but does not concentrate

DIETARY RISK from food and water that uses MRLs and U.S. tolerances			
Chronic non-cancer dietary risk **ADI =0.02 mg/kg bw** **EEC = 2.1 µg/L**	**POPULATION**	**ESTIMATED RISK (% of ADI)**	
		Food	**Food + EEC**
	All infants <1 yr old	47.5	47.6
	Children 1 to 2 yrs	55.7	55.9
	Children 3 to 5 yrs	47.7	47.9
	Children 6 to 12 yrs	32.8	32.1
	Youth 13 to 19 yrs	19.3	19.4
	Adults 20 to 49 yrs	15.4	15.6
	Adults 50+ yrs	12.4	12.5
	Females 13 to 49 yrs	14.5	14.7
	Total Population	20	20.1
Acute dietary exposure analysis, 95th percentile **ARfD = 0.13 mg/kg bw** **EEC = 2.4 µg/L**	**POPULATION**	**ESTIMATED RISK (% of ARfD)**	
		Food	**Food + EEC**
	Females 13+	5.84	5.06
Q*	**Not applicable**		

Appendix III Environmental assessment

Table 1 Fate and behaviour in the terrestrial environment

Property	Test material	Value				Comments
Abiotic transformation						
Hydrolysis	cyclohexane [e-4(6)-^{14}C] labelled tepraloxydim	pH	$t_{1/2}$ in days			Important route under acidic conditions; slow in neutral and alkaline conditions
			22°C	35°C	45°C	
		pH 4: pH 5: pH 7: pH 9:	3.5 24.4 >66 >66	1.4 5.1 56.2 66	0.3 1.1 21.4 16.8	
Phototransformation on soil	cyclohexane[e-4(6)-^{14}C] labelled tepraloxydim	$t_{1/2}$ = 1.1 days				Important route of transformation
Biotransformation						
Biotransformation in aerobic soil	cyclohexane [e-4(6)-^{14}C] labelled tepraloxydim	$t_{1/2}$ = 5.3 days DT_{90} = 17.7 days				non-persistent and is an important route of transformation
	tetrahydropyran ring-labelled tepraloxydim	$t_{1/2}$ = 9 days DT_{90} = 28 days				non-persistent and is an important route of transformation
Biotransformation in anaerobic soil	cyclohexane [e-4(6)-^{14}C] labelled tepraloxydim	$t_{1/2}$ = 3.2 months DT_{90} = 10.5 months water = 3.2 months soil = 3.0 months				moderately persistent
Mobility						
Adsorption in soil	cyclohexane [e-4(6)-^{14}C] labelled tepraloxydim	Soil	K_d	K_{oc}		
		sand	0.011	3.7		very highly mobile
		sandy loam	0.042	8.4		very highly mobile
		loamy sand	0.42	26.5		very highly mobile
		loam	0.53	20.2		very highly mobile
		clay	1.5	77.2		highly mobile
Volatilization	cyclohexane [e-4(6)-^{14}C] labelled tepraloxydim	4 and 8% of the applied amount volatilized from soil and plant surfaces, respectively				low potential for volatilization

Property	Test material	Value	Comments
Field studies			
Field dissipation	BAS 620 00 H (EP)	DT_{50}: Manitoba = 6 d Saskatchewan = 3 d Alberta = 12 d North Dakota = 9 d	non-persistent
		DT_{90}: Manitoba = 36 d Saskatchewan = 20 d Alberta = 76 d North Dakota = 31 d	low potential for carryover
Field leaching		no residues below 5 cm soil depth	low potential for leaching and groundwater contamination

Table 2 Transformation products in the terrestrial environment

Property	Test material	Transformation products	
		Major	Minor
Abiotic transformation			
Hydrolysis	cyclohexane-labelled tepraloxydim	DP-2 (68%) and DP-8 (20%)	DP-6 (2%), DP-10, GP and FP
Phototransformation on soil	cyclohexane-labelled tepraloxydim	DP-1 (11%), GP (22%) and FP (18%)	DP-2 (5%) and DP-6 (4%)
Biotransformation			
Biotransformation in aerobic soil	cyclohexane-labelled tepraloxydim	none	DP-1 (2.8%), DP-2 (7.5%) and DP-4 (2.4%)
	tetrahydropyran ring-labelled tepraloxydim	none	DP-1 (2.8%) and DP-2 (9.2%)
Biotransformation in anaerobic soil	cyclohexane-labelled tepraloxydim	DP-1 (12.1%)	DP-2 and DP-6
Field studies			
Field dissipation	BAS 620 00H (EP)	DP-1 (12% North Dakota site) DP-2 (17% in Alberta site and 15% in North Dakota site)	

( ) maximum concentration of applied radioactivity

Table 3 Fate and behaviour in the aquatic environment

Property	Test material	Value				Comments
Abiotic transformation						
Hydrolysis	cyclohexane[e-4(6)-^{14}C] labelled tepraloxydim	pH	$t_{1/2}$ in days			Important route under acidic conditions; slow in neutral and alkaline conditions
			22°C	35°C	45°C	
		pH 4: pH 5: pH 7: pH 9:	3.5 24.4 >66 >66	1.4 5.1 56.2 66	0.3 1.1 21.4 16.8	
Phototransformation in water	cyclohexane[e-4(6)-^{14}C] labelled tepraloxydim	half-lives: pH 5 = 0.7 d pH 7 = 1.5 d pH 9 = 1.6 d				principal route of transformation
Biotransformation						
Biotransformation in aerobic sediment/water systems	cyclohexane[e-4(6)-^{14}C] labelled tepraloxydim	whole system: $t_{1/2}$ = 48.6–171.4 days DT_{90} = 161.5 days				moderately persistent
		water: $t_{1/2}$ = 41 and 129 days DT_{90} = 136.2 days				slightly to moderately persistent
Biotransformation in anaerobic soil/water systems	cyclohexane[e-4(6)-^{14}C] labelled tepraloxydim	whole system: $t_{1/2}$ = 3.2 months DT_{90} = 10.5 months				moderately persistent
		water $t_{1/2}$ = 3.2 months soil $t_{1/2}$ = 3.0 months				

Table 4 Transformation products in the aquatic environment

Property	Test material	Major	Minor
Abiotic transformation			
Hydrolysis	cyclohexane-labelled tepraloxydim	DP-2 (68%) and DP-8 (20%)	DP-6 (1.7%), DP-10, GP and FP
Phototransformation in water	cyclohexane-labelled tepraloxydim	DP-1 (49.7%), DP-2 (19.2%), DP-6 (13.4%) and GP (20.3%)	DP-4
Biotransformation			
Biotransformation in aerobic sediment/water	cyclohexane-labelled tepraloxydim	DP-1 (11%)	DP-1 and DP-6
Biotransformation in anaerobic soil/water	cyclohexane-labelled tepraloxydim	DP-1 (12.1%)	DP-2 and DP-6

( ) maximum concentration of applied radioactivity

Table 5 Transformation, persistence and mobility of major transformation products in the environment

Transformation product	$t_{½}$ or DT_{50}	Interpretation
DP-1	aquatic phototransformation = 14 days	important route of transformation in the environment
	aquatic aerobic biotransformation = 12.4–43.2 days	non-persistent to slightly persistent in the aquatic environment
	adsorption K_d = 0.47–3.9	moderately to very highly mobile in soils
	field DT_{50} = 28 days	slightly persistent in soils
DP-2	aquatic phototransformation = 6 days soil phototransformation = 4 days	principal route of transformation in the environment
	adsorption K_d = 0.35–14.7	moderately to highly mobile in soils
	field DT_{50} = 198–235 days	persistent under field conditions
DP-6	aquatic phototransformation = 7 days soil phototransformation = 3 days	important route of transformation in the environment
GP	soil phototransformation = 12 days	may be a route of transformation in the environment

Table 6 Effects on terrestrial organisms

Organism	Exposure	Test material	Endpoint value		Degree of toxicity
			NOEC/NOEL	LC_{50}/EC_{50}	
Invertebrates					
Earthworm	acute (mg/kg)	Tepraloxydim	NOEC = 400 a.i.	LC_{50} >1000	
		EP	NOEC = 781 EP	LC_{50} >1390 EP	
		EP + Dash HC	NOEC = 63 EP + 225 Dash HC	LC_{50} = 120.3 EP + 437 Dash HC	
Bee	oral (µg/bee)	Tepraloxydim	NOEC = 10 a.i.	LC_{50} >25 a.i.	non-toxic
		EP + Dash HC	NOEC = 30 EP + 120 Dash HC	LC_{50}>40 EP + 160 Dash HC	non-toxic
	contact (µg/bee)	EP + Dash HC	NOEC = 40 EP + 160 Dash HC	LC_{50}>40 EP + 160 Dash HC	non-toxic
Birds					
Bobwhite quail	acute (mg a.i./kg bw)	Tepraloxydim	NOEL = 500	LD_{50} >2000	practically non-toxic
	dietary (mg a.i./kg diet)	Tepraloxydim	NOEC = 1464	LC_{50} >5869	practically non-toxic
	reproduction (mg a.i./kg diet)	Tepraloxydim	NOEC = 1000		no effect up to 1000 mg a.i./kg diet
Mallard duck	dietary (mg a.i./kg diet	Tepraloxydim	NOEC = 745	LC_{50} >5914	practically non-toxic
Mammals					
Rat	acute (mg a.i./kg bw)	Tepraloxydim	not available	LD_{50} >2000	practically non-toxic
	dietary (mg a.i./kg diet)	Tepraloxydim	NOEC = 500 (28-day) NOEC = 300 (90-day)	not available	
	reproduction (mg a.i./kg diet)	Tepraloxydim	NOEC = 500		no effect up to 500 mg a.i./kg diet
Mouse	dietary (mg a.i./kg diet)	Tepraloxydim	NOEC = 1200 (90-day)	not available	

Organism	Exposure	Test material	Endpoint value		Degree of toxicity
			NOEC/NOEL	LC_{50}/EC_{50}	
Vascular plants					
Vascular plant	seedling emergence: ryegrass dry weight (g EP + 858.28 g Dash HC)*	EP + Dash HC	NOEC = 28.2 EP	EC_{25} = 91.3 EP	phytotoxic effect observed
	vegetative vigour: corn dry weight* (g EP + 858.28 Dash HC)*	EP + Dash HC	NOEC = 9.4 EP	EC_{25} = 25.2 EP	phytotoxic effect observed

* most sensitive species and parameter

Table 7 Effects on aquatic organisms

Organism	Exposure	Test material	Endpoint value (mg/L)		Degree of toxicity[a]
			NOEC	LC_{50}/EC_{50}	
Freshwater species					
Daphnia sp	Acute	Equinox (EP)	NOEC = 2.89 EP	LC_{50} = 7.44 EP	moderately toxic
Rainbow trout	Acute	Tepraloxydim	NOEC = 48.2 a.i.	LC_{50} >100 a.i.	non-toxic
		Equinox (EP)	NOEC = 0.45 EP	LC_{50} = 4.45 EP	moderately toxic
		Equinox (EP) +Dash HC	NOEC = 0.43 EP + 0.83 Dash HC	LC_{50} = 0.91EP + 1.92 Dash HC	moderately toxic
Bluegill sunfish	Acute	Tepraloxydim	NOEC = 44.8 a.i.	LC_{50} = 78.2 a.i.	slightly toxic
Bioconcentration in fish		Tepraloxydim	BCF = 2.3 (max)	depuration half-life = 0.92 days	low potential
Freshwater alga—green alga	Acute	Tepraloxydim	NOEC = 10.2 a.i.	EC_{50} = 21.9 a.i.	
		Equinox (EP)	NOEC = 0.4 EP	EC_{50} = 5.1 EP	
		Equinox (EP) +Dash HC	NOEC = 1.4 EP + 5.0 Dash HC	EC_{50} = 5.6 EP + 19.9 Dash HC	
Freshwater alga—blue-green alga	Acute	Tepraloxydim	NOEC = 25.5 a.i.	EC_{50} = 108 a.i.	

Organism	Exposure	Test material	Endpoint value (mg/L)		Degree of toxicity[a]
			NOEC	LC_{50}/EC_{50}	
Plants: *Lemna* sp	Acute (Tier 1)	Equinox (EP)	NOEC = 0.482	EC_{50} = 0.482	
	Acute (Tier 2)	Tepraloxydim	NOEC = 1.11	EC_{50} = 6.47	
Marine species					
Crustacean (Mysid shrimp)	Acute	Tepraloxydim	NOEC = 120 a.i.	LC_{50} >120 a.i.	practically non-toxic
		Equinox (EP)	NOEC <0.26 EP	LC_{50} = 1.35 EP	moderately toxic
Mollusk (Eastern oyster)	Acute	Tepraloxydim	NOEC = 73 a.i.	EC_{50} >120 a.i.	practically non-toxic
		Equinox (EP)	NOEC = 0.36 EP	EC_{50} = 0.5 EP	highly toxic
Sheepshead minnow	Acute	Tepraloxydim	NOEC = 120 a.i.	LC_{50} >120 a.i.	practically non-toxic
		Equinox (EP)	NOEC = 3.1 EP	LC_{50} = 7.17 EP	moderately toxic
Marine diatom	Acute	Tepraloxydim	NOEC = 0.55 a.i.	LC_{50} = 1.03 a.i.	

[a] USEPA classification, where applicable

Table 8 Risk to terrestrial organisms

Organism	EEC	Test material	Endpoint	RQ	Risk
Invertebrates					
Earthworm	0.022 mg a.i./kg soil	Tepraloxydim	NOEC = 400 mg a.i./kg soil	<0.001	none
	0.115 mg EP/kg soil	EP	NOEC = 781.3 mg EP/kg soil	<0.001	none
	0.369 mg EP + Dash HC /kg soil	EP + Dash HC	NOEC = 288 mg EP + Dash HC/kg soil	0.001	none
Bee	50 g a.i./ha (appl. rate)	Tepraloxydim	NOEC = 10 µg a.i./bee (11.2 kg a.i./ha)	0.005	none
	824.4 g EP + Dash HC/ha (appl. rate)	EP + Dash HC	NOEC = 200g EP + Dash HC µg/bee 224 kg EP + Dash HC kg/ha	0.004	none
Birds					
Bobwhite quail	DI: 0.13 mg a.i./ind/d	Tepraloxydim	acute NOEL = 500 mg a.i./kg bw	648 days	none
	8.75 mg a.i./kg diet	Tepraloxydim	dietary NOEC = 1464 mg a.i./kg diet	0.010	none
	8.75 mg a.i./kg diet	Tepraloxydim	reproduction NOEC = 1000 mg a.i./kg diet	0.010	none
Mallard duck	1.69 mg a.i./kg diet	Tepraloxydim	dietary NOEC = 745 mg a.i./kg diet	0.002	none
Mammals					
Rat	DI= 1.51mg a.i./ind/d	Tepraloxydim	acute NOEL = 200 mg a.i./kg bw ($1/10^{th}$ of LD_{50} of 2000 mg a.i./kg bw)	46 days	none
	25.22 mg a.i./kg diet	Tepraloxydim	dietary NOEC = 300 mg a.i./kg diet	0.080	none
	25.22 mg a.i./kg diet	Tepraloxydim	reproduction NOEC = 500 mg a.i./kg diet	0.050	none
Mouse	25.07 mg a.i./kg diet	Tepraloxydim	dietary NOEC = 1200 mg a.i./kg diet	0.020	none

Organism	EEC	Test material	Endpoint	RQ	Risk
Vascular plants					
Plants	Seedling emergence	258 EP + 570.4 Dash HC g/ha	EC_{25} = 91.3 EP + 858.28 Dash HC g/ha	0.870	no risk
	Vegetative vigour	258 EP + 570.4 Dash HC g/ha	EC_{25} = 25.2 EP + 858.28 Dash HC g/ha	0.940	no risk

* most sensitive species and parameter

Table 9 Risk to aquatic organisms

Organism	Exposure 0.033 mg a.i./L 0.172 mg EP/L 0.552 EP + Dash HC mg/L	Toxicity endpoint mg/L	RQ	Risk
Freshwater species				
Daphnia sp	EP	Acute NOEC: 2.89 EP	0.060	none
Rainbow trout	Tepraloxydim	Acute NOEC: 48.2 a.i.	0.001	none
	EP	Acute NOEC: 0.45 EP	0.380	none
	EP + Dash HC	Acute NOEC: 1.26 (EP + Dash HC)	0.440	none
Bluegill sunfish	Tepraloxydim	Acute NOEC: 44.8 a.i.	0.001	none
Bioconcentration in fish	Tepraloxydim	Depuration half-life: 0.92 d	BCF: 2.3	none
Freshwater green algae*	Tepraloxydim	NOEC: 10.2 a.i.	0.003	none
	EP	NOEC: 0.4 EP	0.430	none
Plants: *Lemna* sp	Tepraloxydim	NOEC: 1.11 a.i.	0.030	none

* most susceptible species

References

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